

\_\_\_\_\_

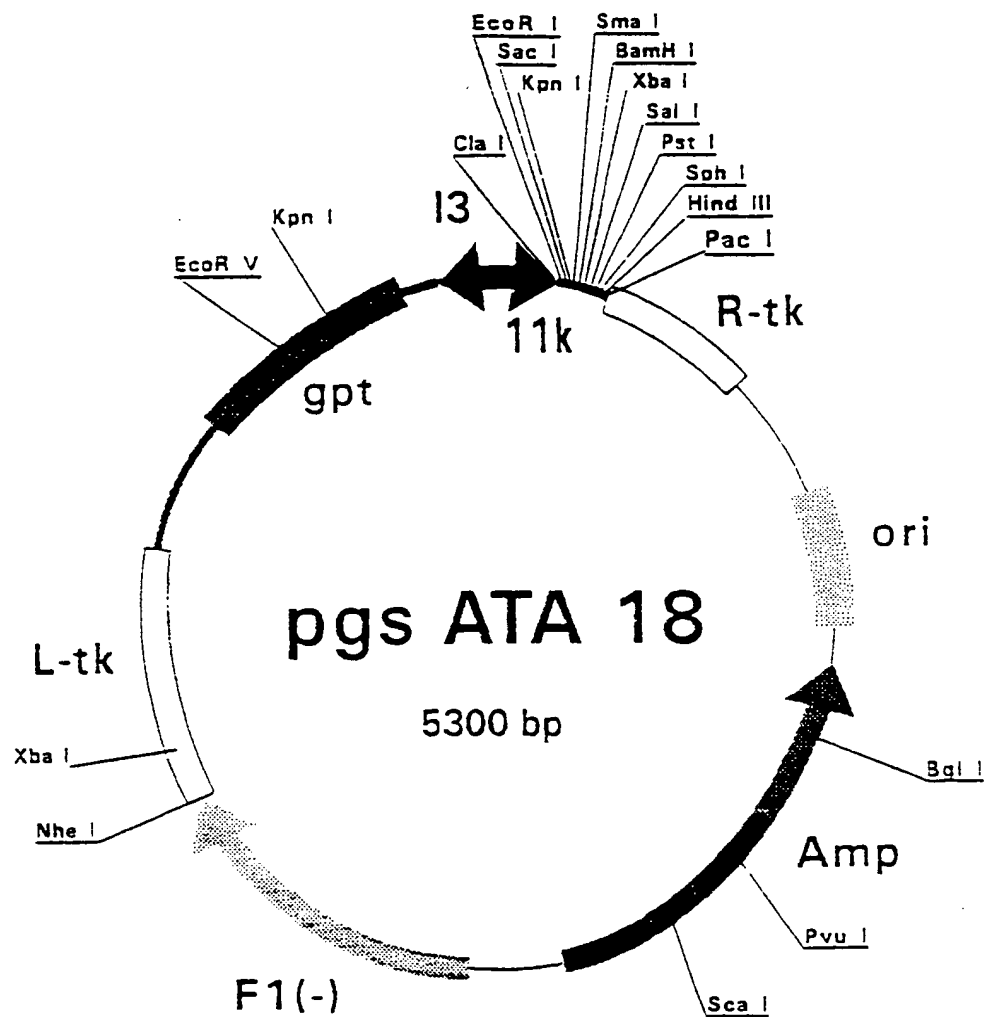


Fig. 2

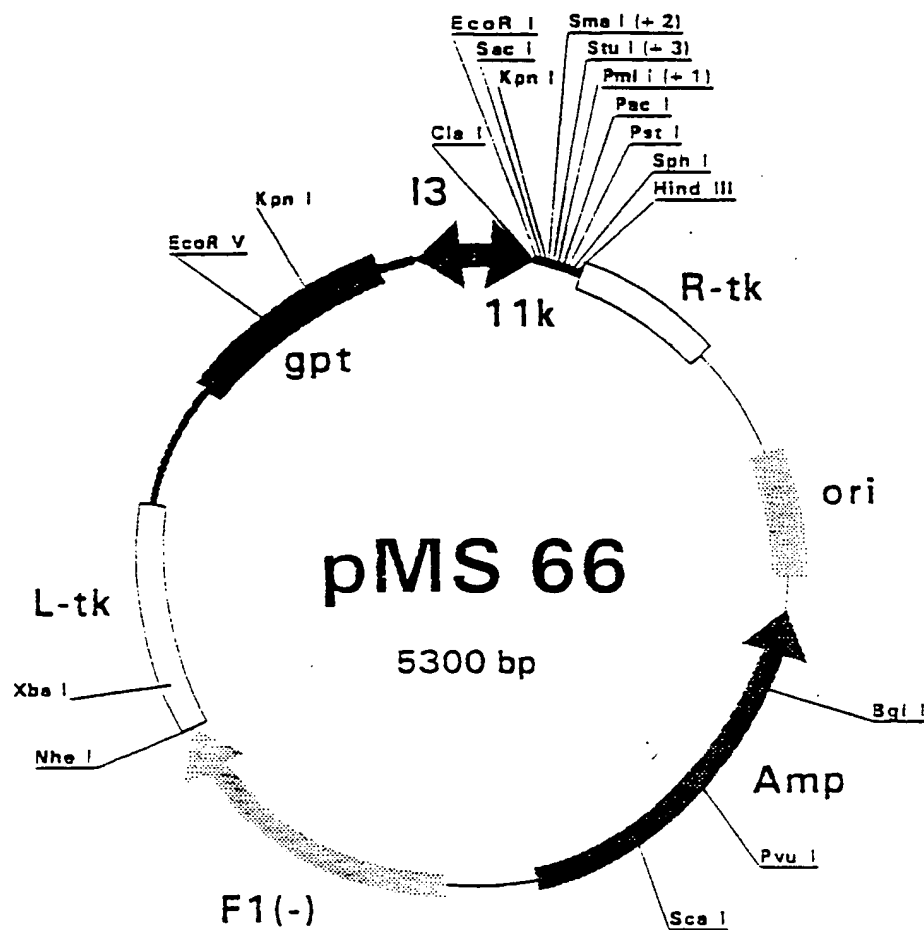


Fig. 3

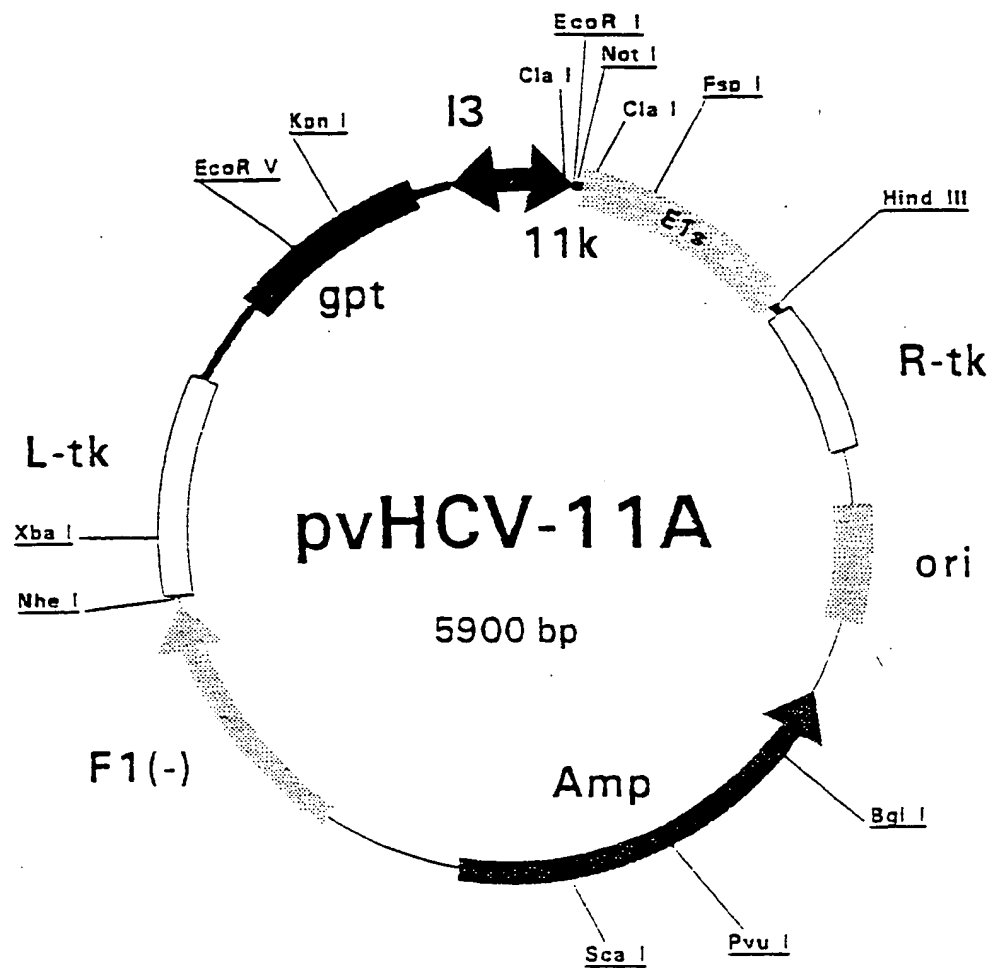
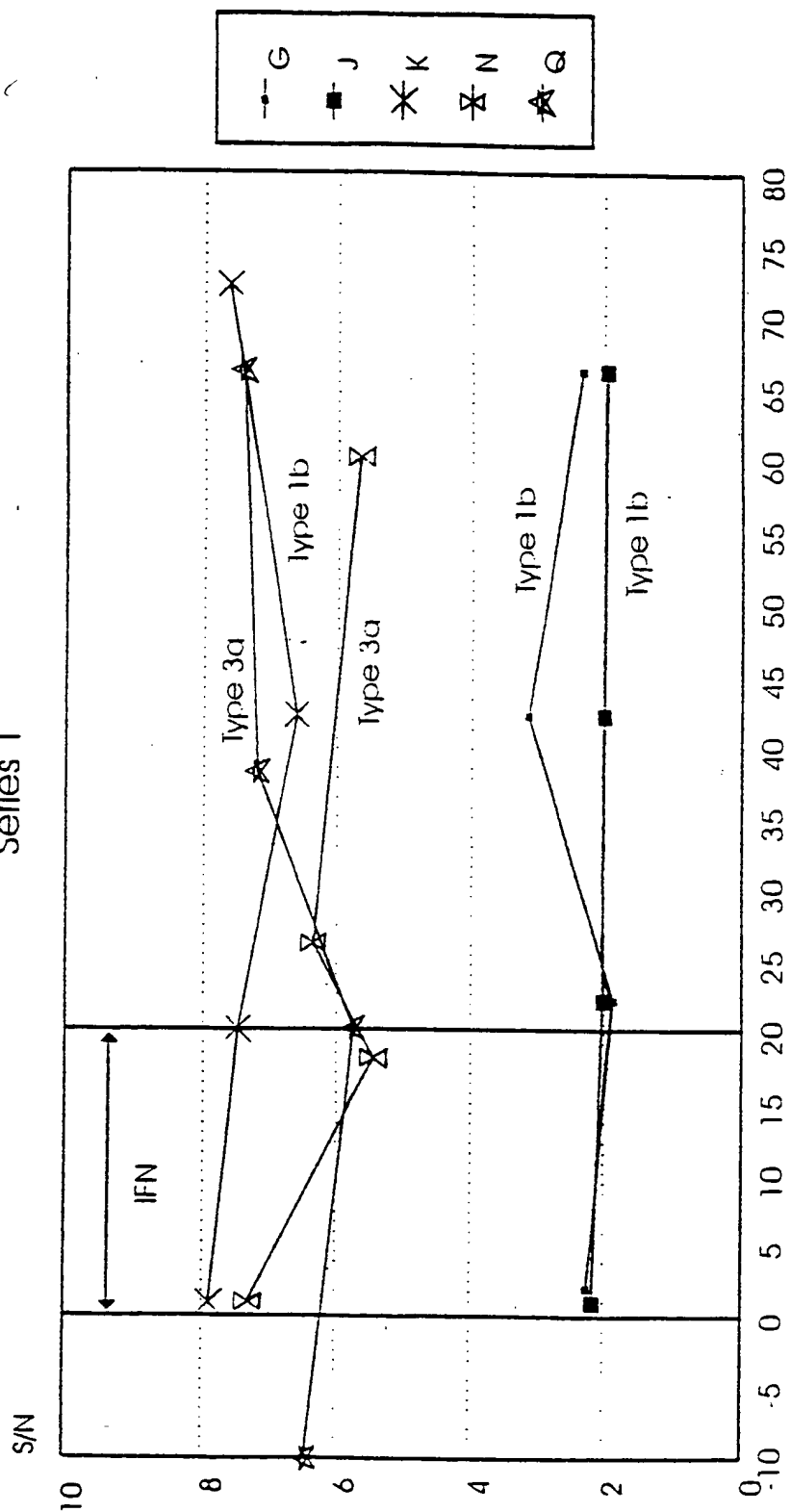


Fig. 4

# Anti-E1 levels in NON-responders to IFN treatment

Series 1

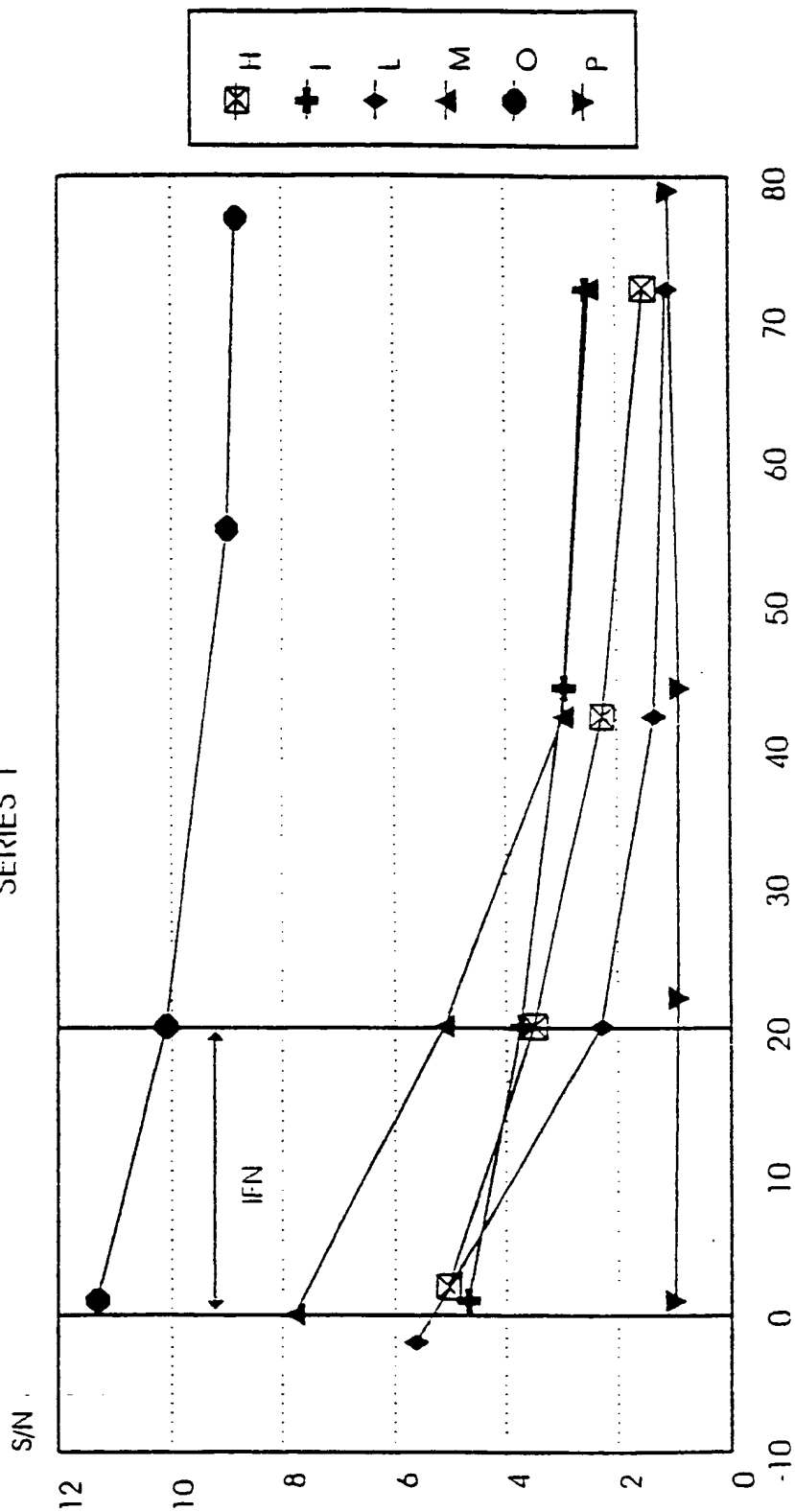


weeks after start of treatment

Fig. 5

# Anti-E1 levels in RESPONDERS to IFN treatment

SERIES 1

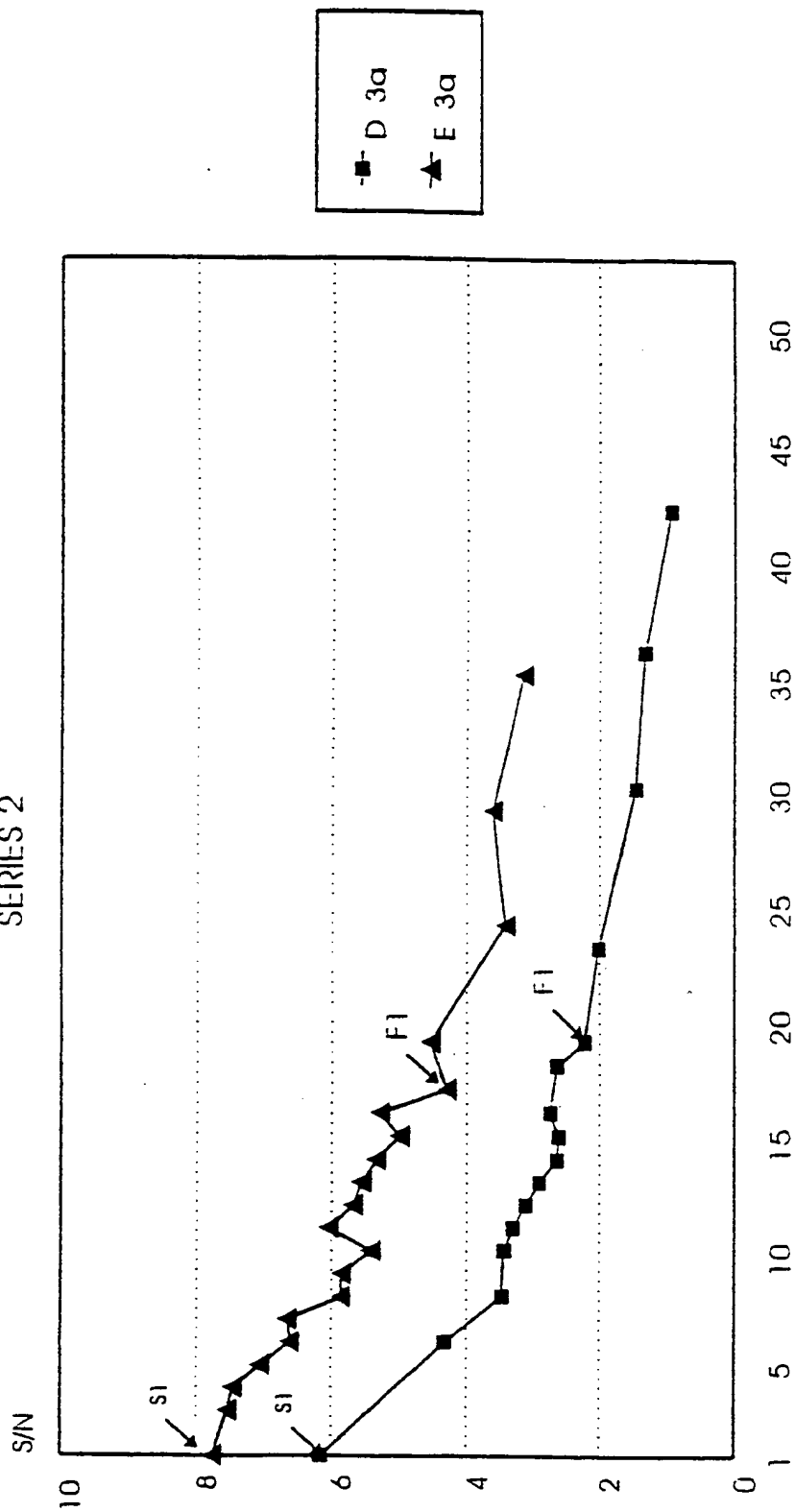


weeks after start of treatment

Fig. 6

# Anti-E1 levels in patients with COMPLETE response to IFN

SERIES 2

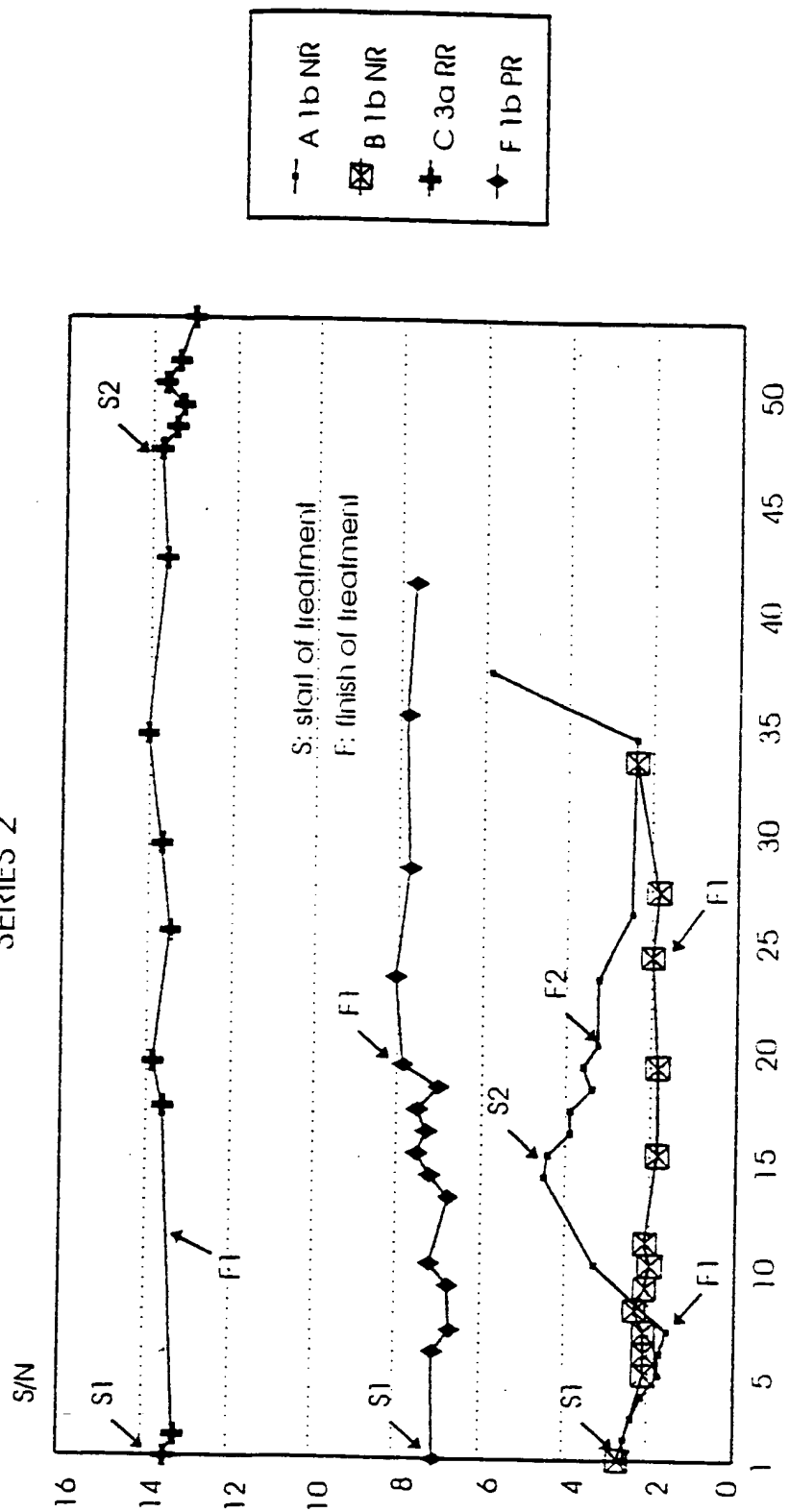


months after start of treatment

Fig. 7

# Anti-E1 levels in INCOMPLETE responders to IFN treatment

SERIES 2



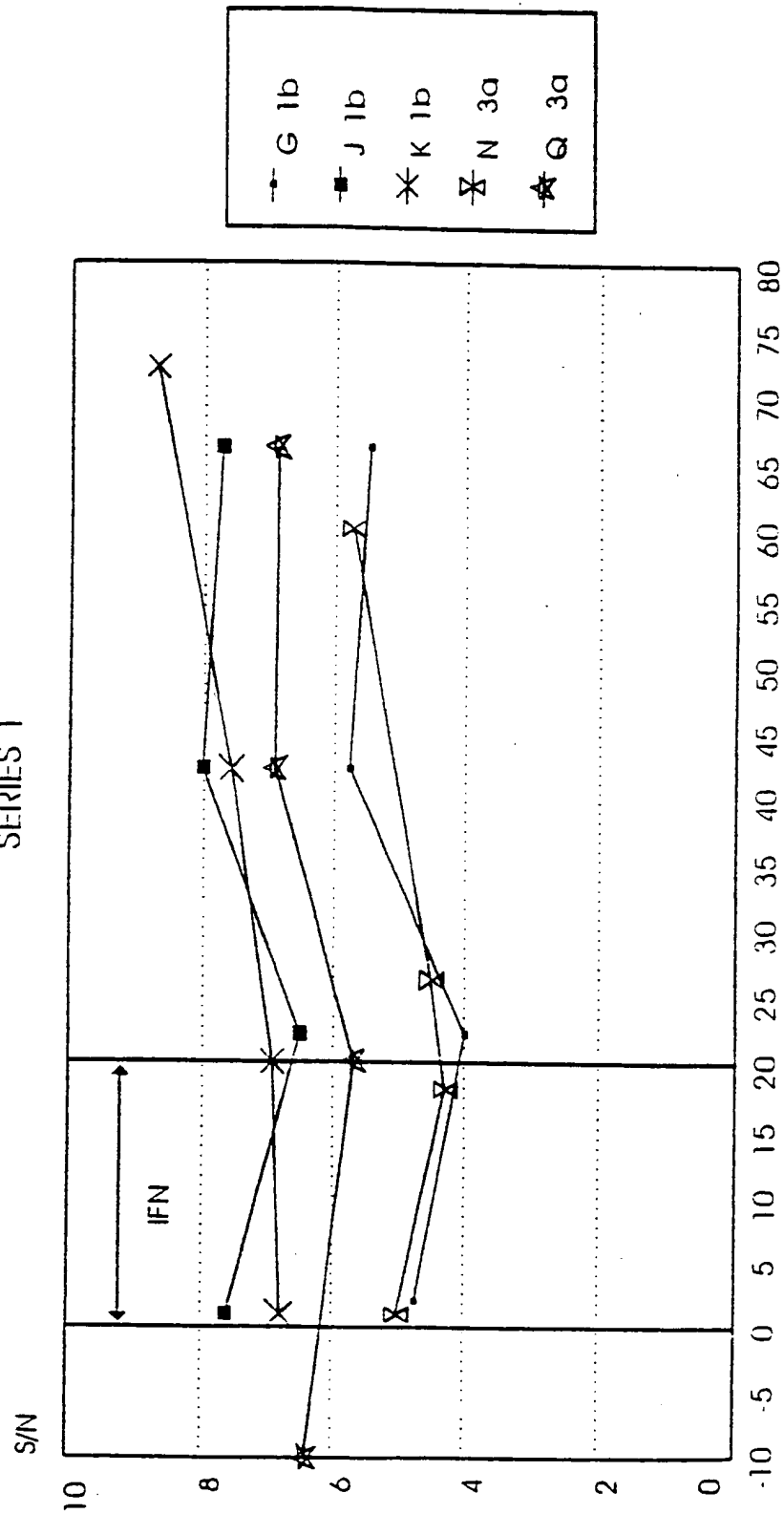
months after start of treatment

Fig. 8



# Anti-E2 levels in NON-RESPONDERS to IFN treatment

SERIES 1

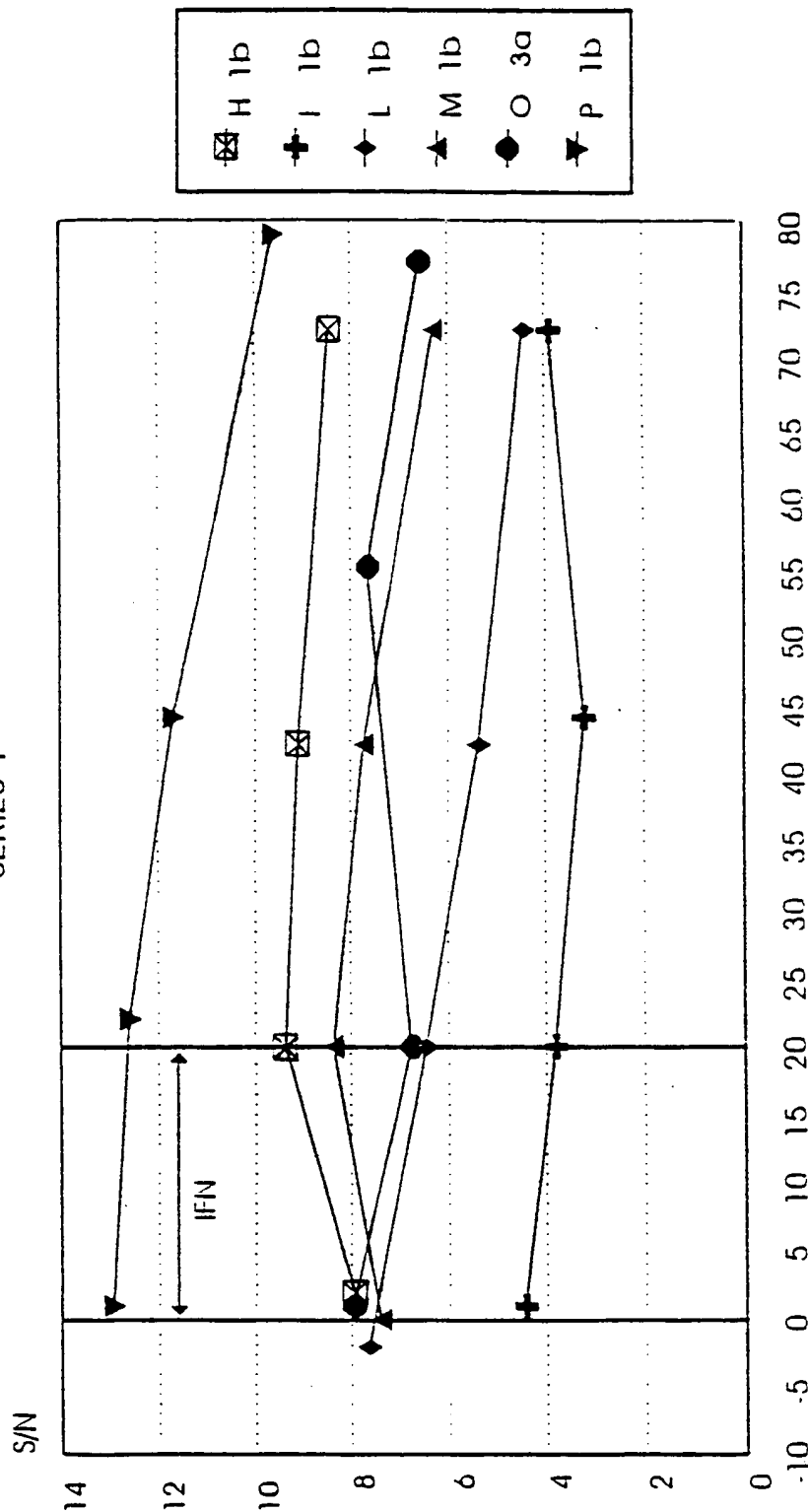


weeks after start of treatment

Fig. 9

# Anti-E2 levels in RESPONDERS to IFN treatment

SERIES 1



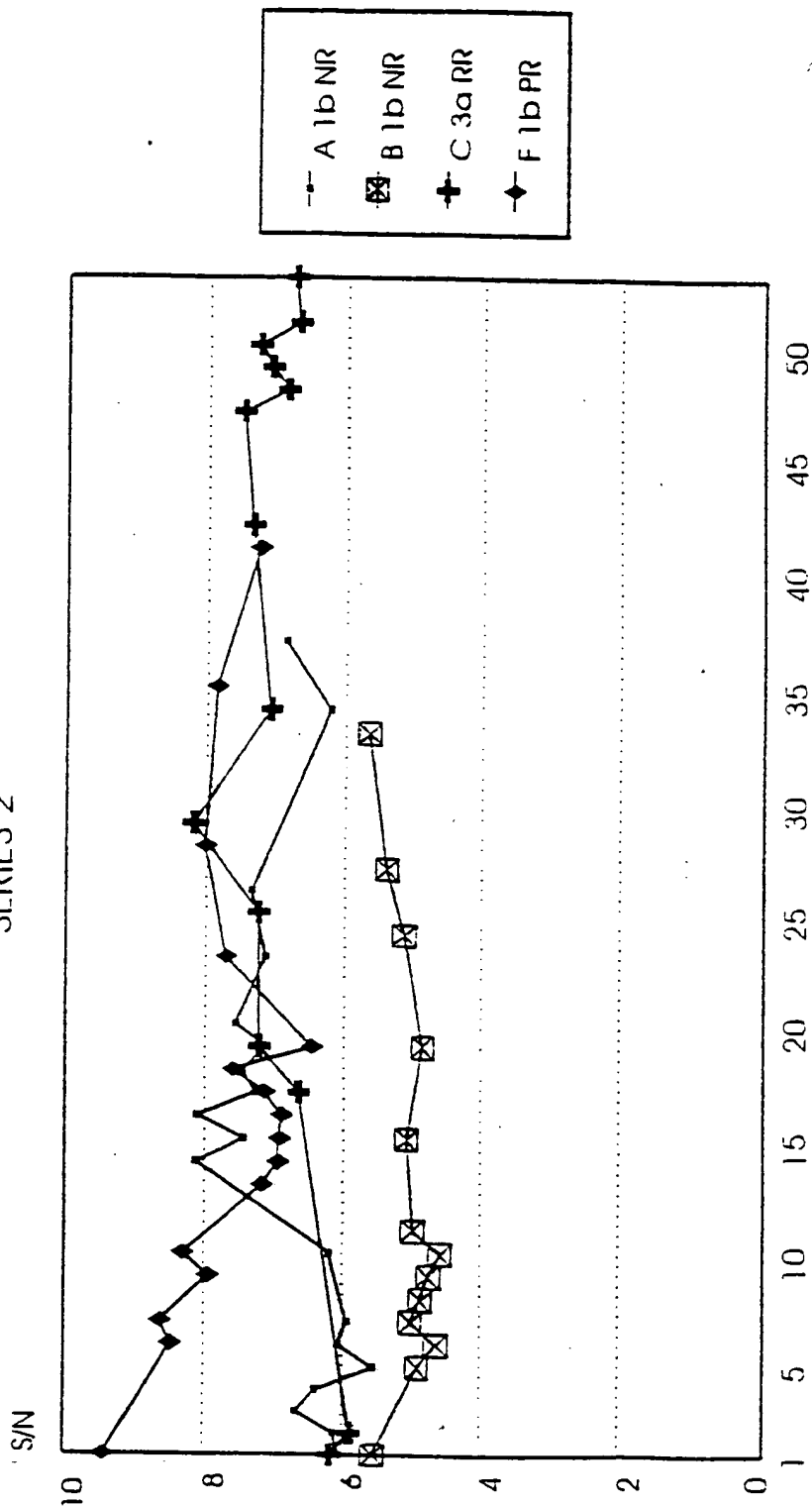
weeks after start of treatment

Fig.10

FIGURE 11

# Anti-E2 levels in INCOMPLETE responders to IFN treatment

SERIES 2



months after start of treatment

Fig.11

# Anti-E2 levels in COMPLETE responders to IFN treatment

SERIES 2

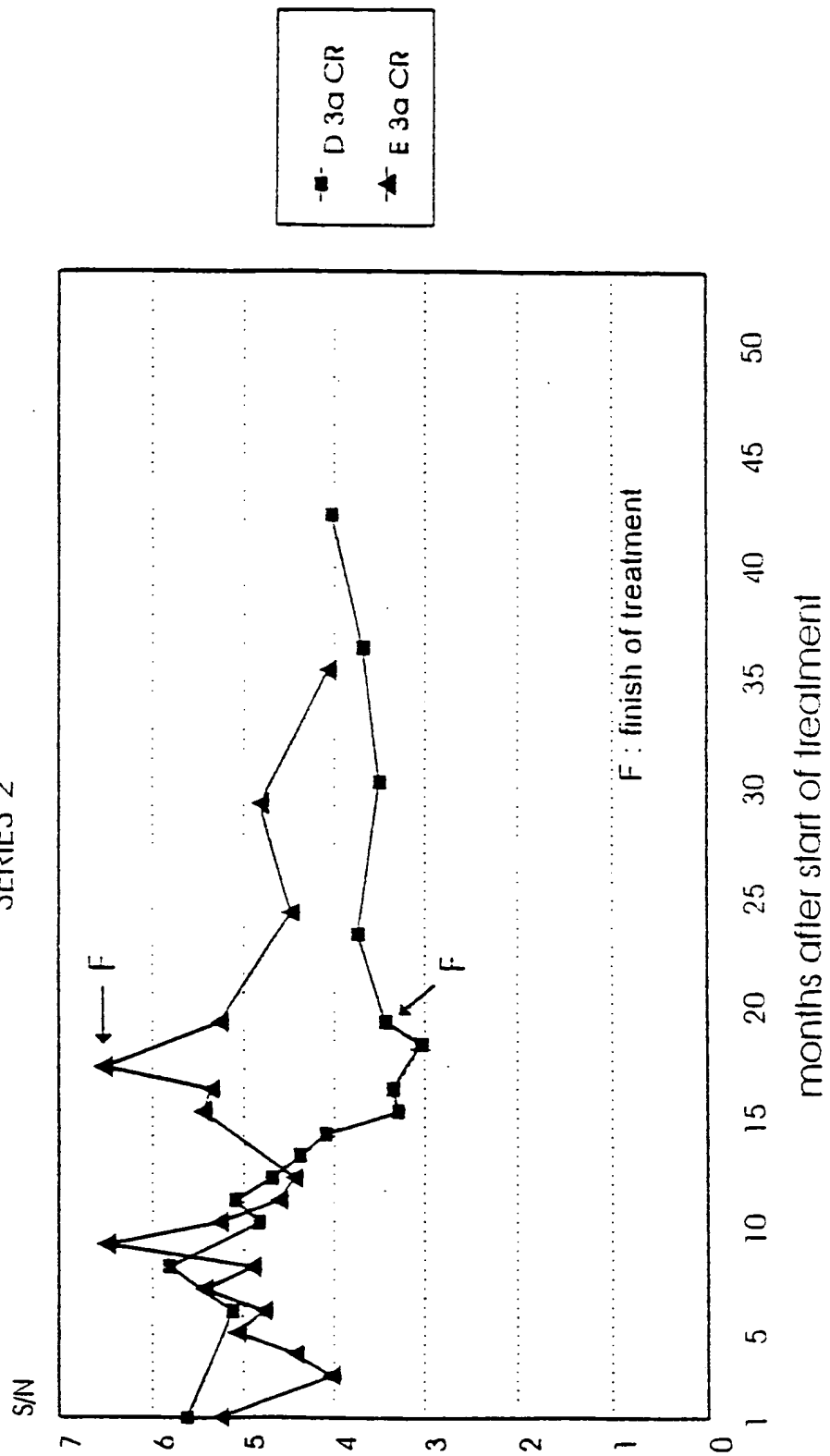
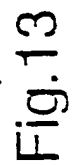


Fig.12



# Competition of reactivity of anti-E1 Mabs with peptides

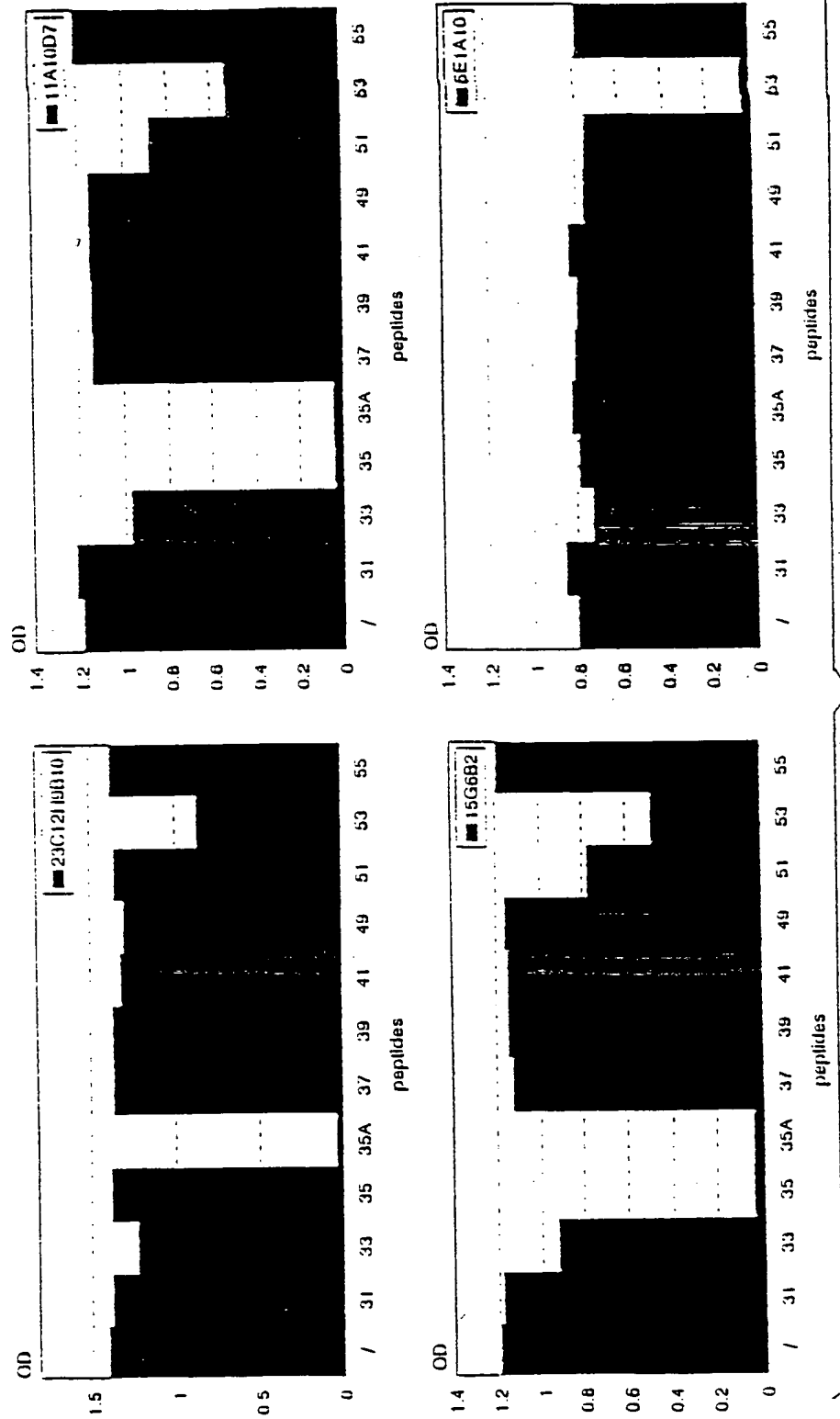
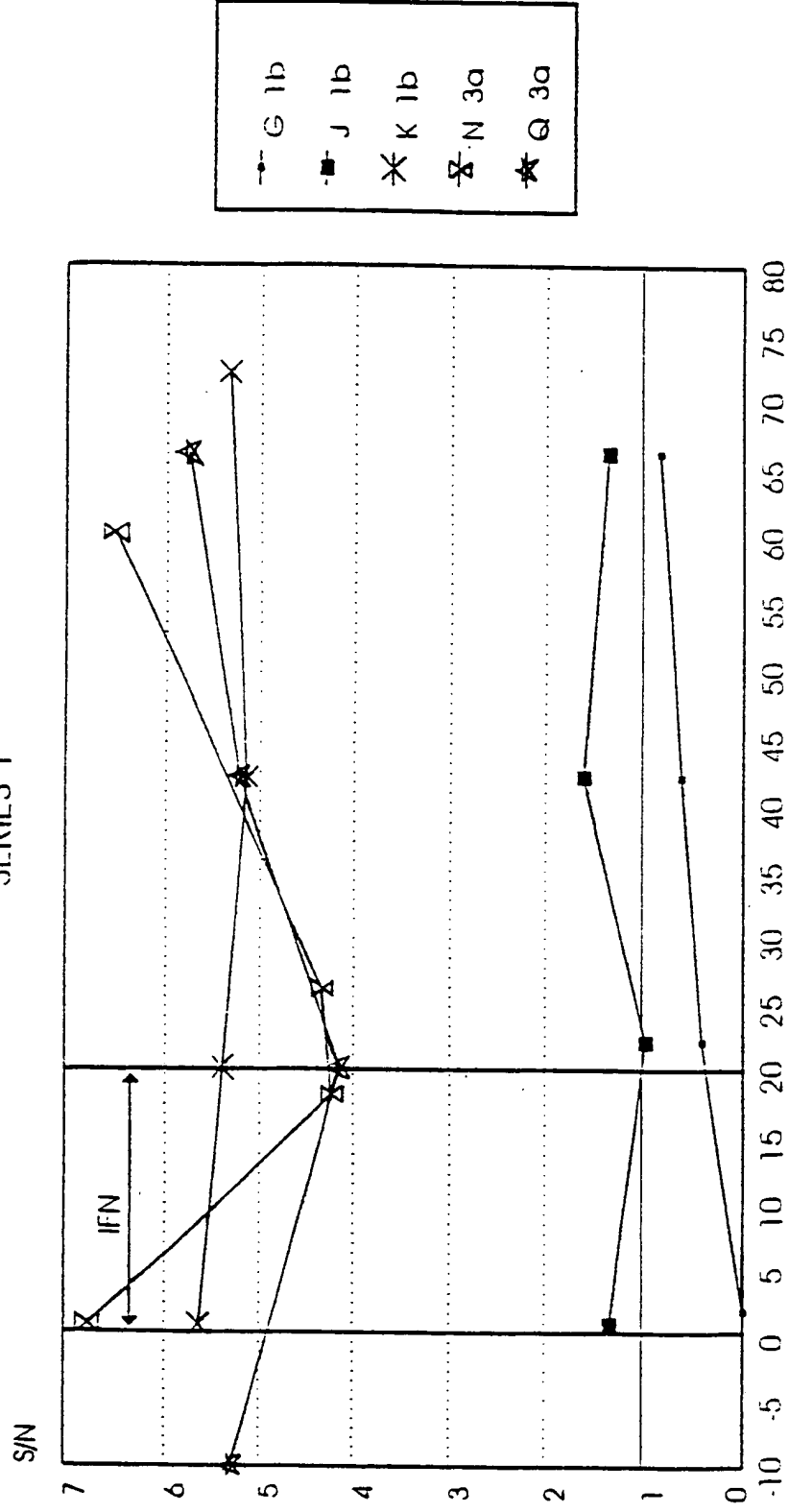


Fig.14

# Anti-E7 (epitope 1) levels in NON-RESPONDERS to IFN treatment

SERIES 1



weeks after start of treatment

Fig.15

# Anti-E1 (epitope 1) levels in RESPONDERS to IFN treatment

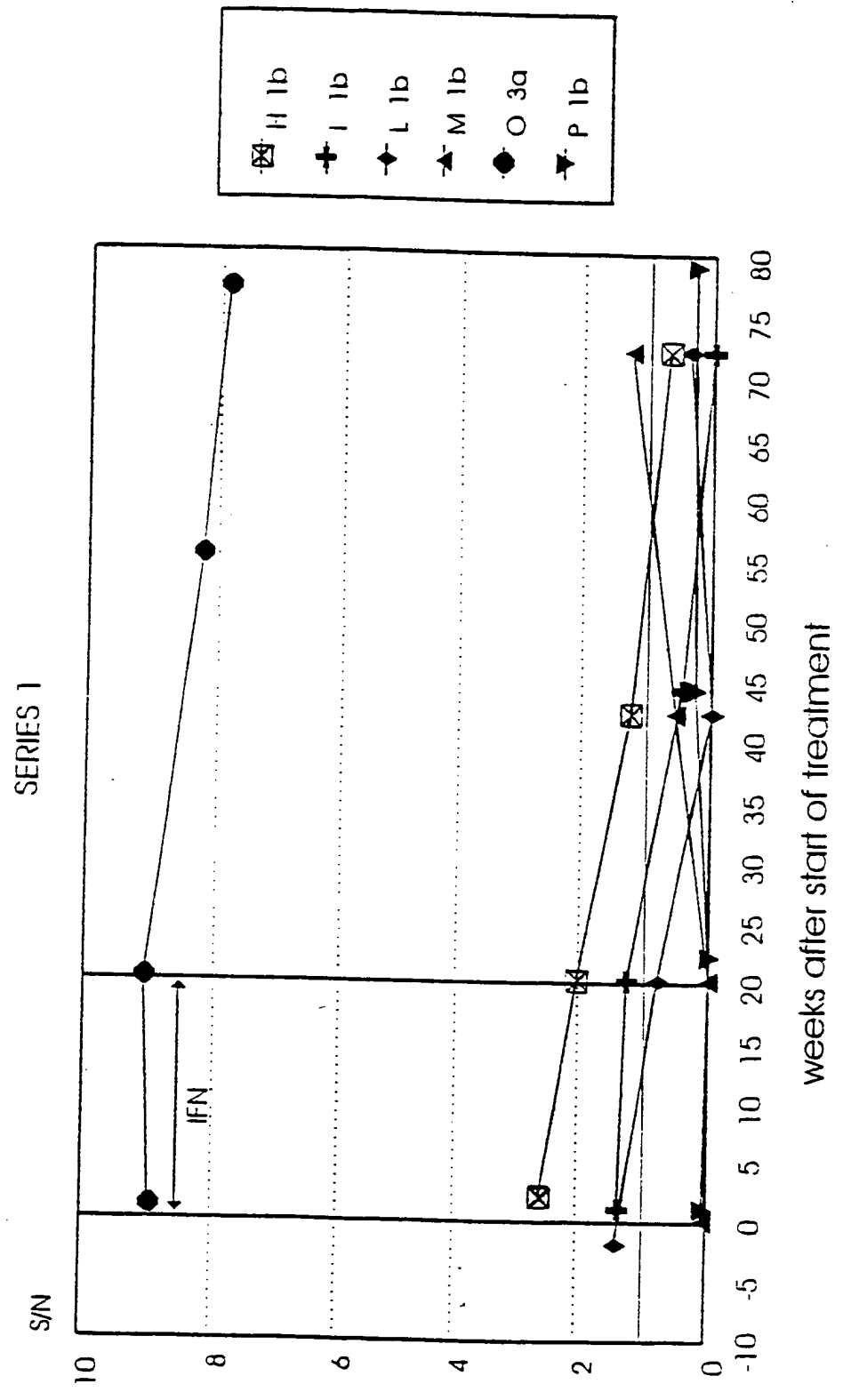


Fig.16



# Anti-E1 (epitope 2) levels in NON-RESPONDERS to IFN treatment

SERIES 1

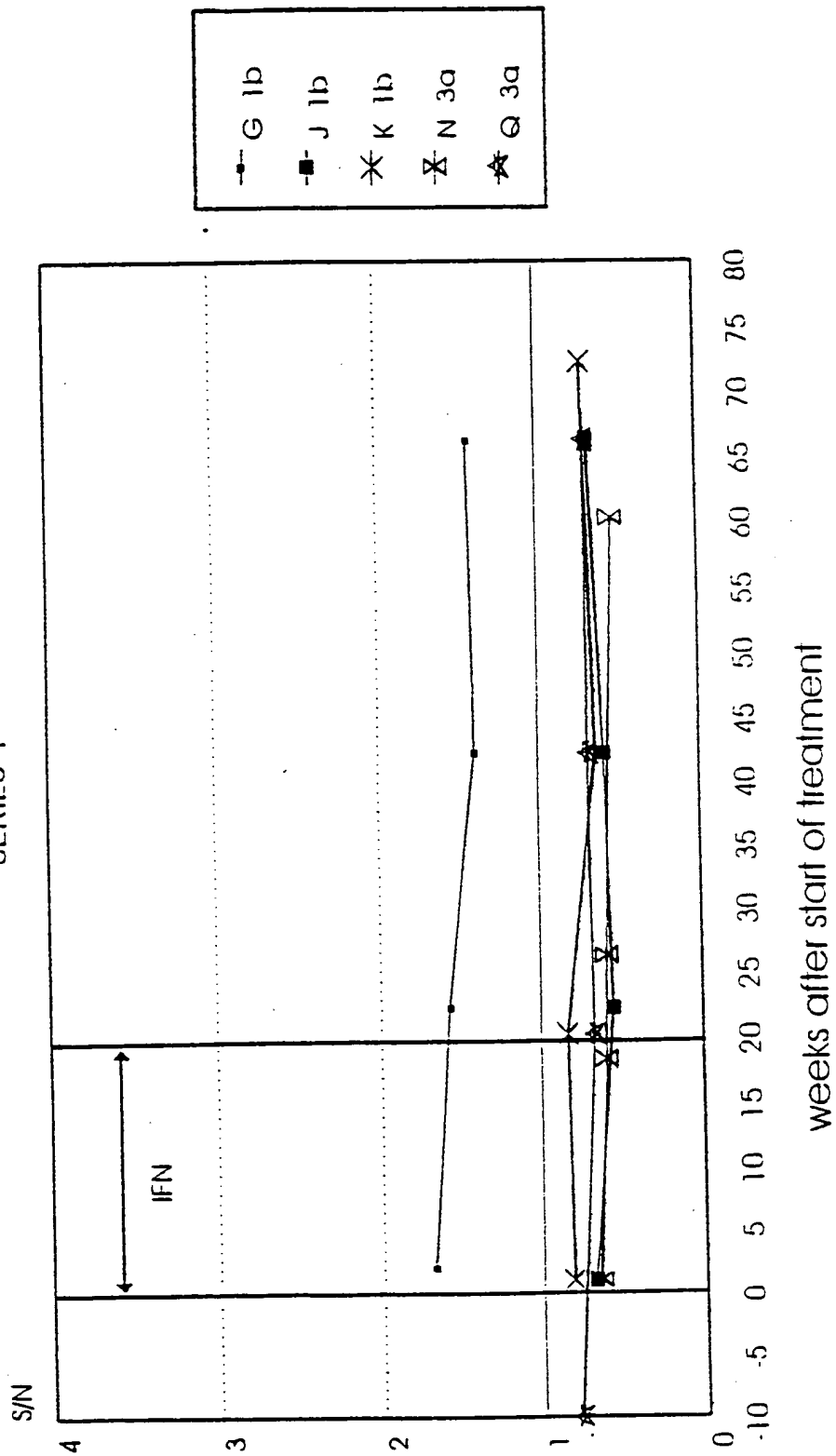


Fig.17

# Anti-E1 (epitope 2) levels in RESPONDERS to IFN treatment

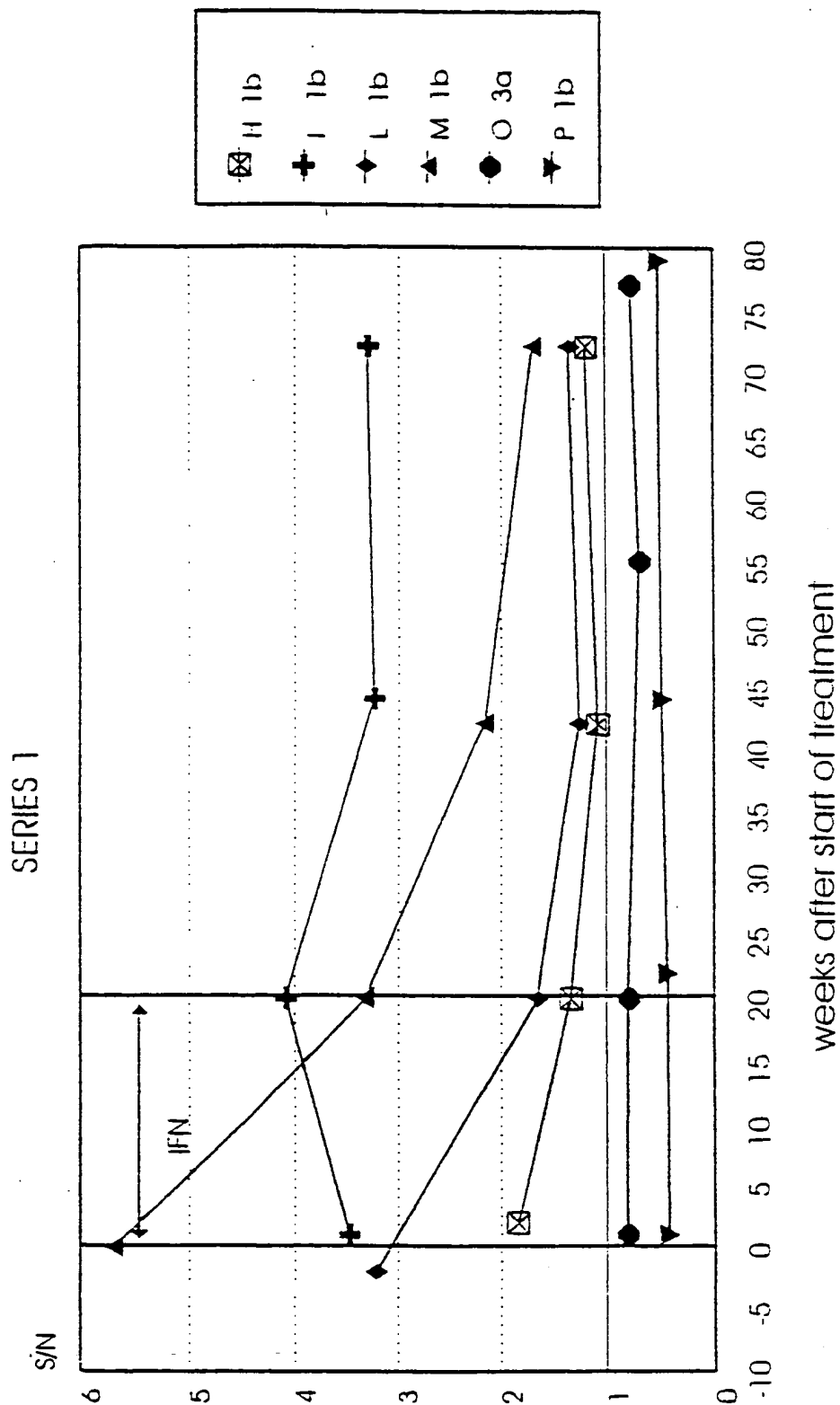


Fig.18

# Competition of reactivity of anti-E2 Mabs with peptides

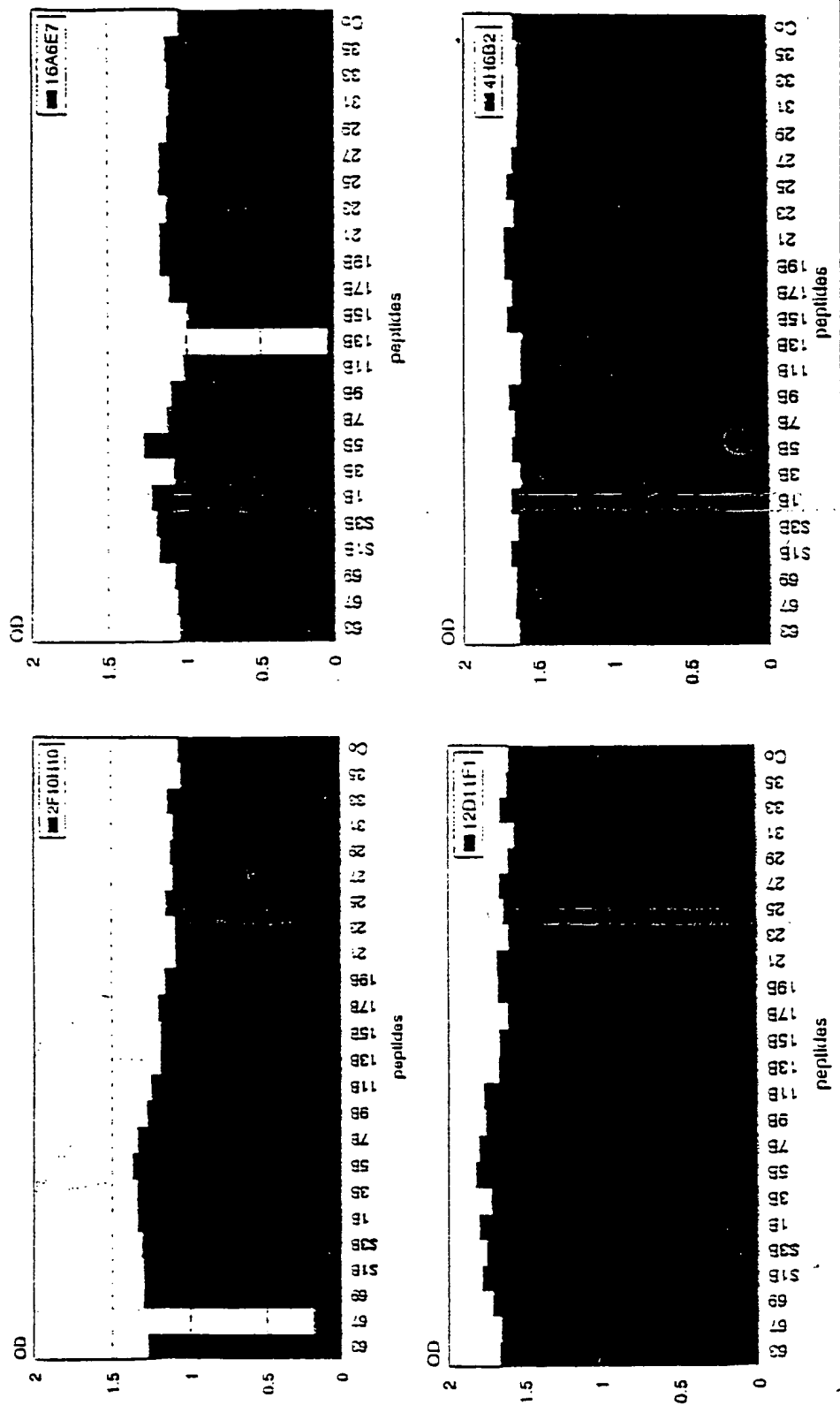
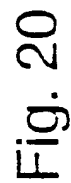


Fig.19



## Fig. 21A

5' GGCATGCAAGCTTAATTAATT3' (SEQ ID NO 1)

3'ACGTCCGTACGTTTGAATTAATTAATCGA5' (SEQ ID NO 94)

5'CCGGGGAGGGCCTGCACGTGATCGAGGGCAGACACCATCACCACCATCACTAATAGT  
TAATTAAGTCA 3' (SEQ ID NO 2)

3'CCTCCGGACGTGCACTAGCTCCCGTCTGTGGTAGTGGTGGTAGTGATTATCAATTAATTG  
5' (SEQ ID NO 95)

SEQ ID NO 3 (HCC19A)

ATGCCCGGTTGCTCTTTCTCTATCTTCTTGGCTTTACTGTCTGTCTGACCAATTCOA  
GCTTCCGCTTATGAGGTGCGCAACGTGTCCGGGATGTACCATGTCACGAACGACTGCT  
CCAACTCAAGCATTGTGTATGAGGCAGCGGACATGATCATGCACACCCCCGGGTGCGT  
GCCCTGCGTTCCGGGAGAACAACTCTTCCCGCTGCTGGGTAGCGCTCACCCCCACGCTC  
GCAGCTAGGAACGCCAGCGTCCCCACCACGACAATACGACGCCACGTGATTTGCTCG  
TTGGGGCGGGCTGCTCTCTGTTCCGCTATGTACGTGGGGGATCTCTGCGGATCTGTCTTC  
CTCGTCTCCAGCTGTTACCATCTCGCCTCGCCGGCATGAGACGGTGCAGGACTGCA  
ATTGCTCAATCTATCCCGGCCACATAACAGGTCACCGTATGGCTTGGGATATGATGAT  
GAACTGGTCGCCTACAACGGCCCTGGTGGTATCGCAGCTGCTCCGGATCCCACAAGCT  
GTCGTGGACATGGTGGCGGGGGCCCATTTGGGGAGTCCTGGCGGGGCTCGCCTACTATT  
CCATGGTGGGGAAGTGGGCTAAGGTTTTGATTGTGATGCTACTCTTTGCTCTCTAATAG

SEQ ID NO 5 (HCC110A)

ATGTTGGGTAAAGTCATCGATACCCTTACATGCGGCTTCGCCGACCTCGTGGGGTACA  
TTCCGCTCGTCGGCGCCCCCTAGGGGGCGCTGCCAGGGGCCCTGGCGCATGGCGTCCG  
GGTTCTGGAGGACGGCGTGAAGTATGCAACAGGGAATTTGCCCGGTTGCTCTTTCTCT  
ATCTTCTCTTGGCTTTGCTGTCTGTCTGACCGTTCCAGCTTCCGCTTATGAAGTGGC  
CAACGTGTCCGGGATGTACCATGTCACGAACGACTGCTCCAACTCAAGCATTGTGTAT  
GAGGCAGCGGACATGATCATGCACACCCCCGGGTGCGTGCCTTCCGTTCCGGGAGAAC  
AACTCTTCCCGCTGCTGGGTAGCGCTCACCCCCACGCTCGCAGCTAGGAACGCCAGCG  
TCCCCACCACGACAATACGACGCCACGTGATTTGCTCGTTGGGGCGGGCTGCTTTCTG

Year	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100
1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100	

SEQ ID NO 7 (HCC111A)

SEQ ID NO 9 (HCC112A)

SEQ ID NO 11 (HCC113A)

ATGTCCGGTTGCTCTTTCTCTATCTTCCTCTTGGCCCTGCTGTCTGTCTGACCATACCA  
GCTTCCGCTTATGAAGTGCGCAACGTGTCCGGGGTGTACCATGTCACGAACGACTGCT  
CCAACTCAAGCATAGTGTATGAGGCAGCGGACATGATCATGCACACCCCGGGGTGCGT

Fig. 21C

GCCCTGCGTTGCGGAGGGCAACTCCTCCCGTTGCTGGGTGGCGCTCACTCCCACGCTC  
GCGGCCAGGAACGCCAGCGTCCCCACAACGACAATACGACGCCACGTCGATTTGCTC  
GTTGGGGCTGCTGCTTTCTGTTCCGCTATGTACGTGGGGGATCTCTGCGGATCTGTTTT  
CCTTGTTTTCCAGCTGTTACCTTCTCACCTCGCCGGCATCAAACAGTACAGGACTGCA  
ACTGCTCAATCTATCCCGGCCATGTATCAGGTACCGCATGGCTTGGGATATGATGAT  
GAACTGGTAATAG

SEQ ID NO 13 (HCC17A)

ATGCTGGGTAAGGCCATCGATACCCTTACGTGCGGCTTCGCCGACCTCGTGGGGTACA  
TTCCGCTCGTCGGCGCCCCCTAGGGGGCGCTGCCAGGGCCCTGGCGCATGGCGTCCG  
GGTTCTGGAAGACGGCGTGAACATGCAACAGGGAATTTGCCTGGTTGCTCTTTCTCTA  
TCTTCCTCTTGGCTTTACTGTCTGTCTAACCATTCCAGCTTCCGCTTACGAGGTGCGC  
AACGTGTCCGGGATGTACCATGTACGAACGACTGCTCCAACCTCAAGCATTGTGTATG  
AGGCAGCGGACATGATCATGCACACCCCCGGGTGCGTGCCCTGCGTTCGGGAGAACA  
ACTCTTCCCGCTGCTGGGTAGCGCTCACCCCCACGCTCGCGGCTAGGAACGCCAGCAT  
CCCCACTACAACAATACGACGCCACGTCGATTTGCTCGTTGGGGCGGCTGCTTTCTGTT  
CCGCTATGTACGTGGGGGATCTCTGCGGATCTGTCTTCCTCGTCTCCAGCTGTTCCACC  
ATCTCGCCTCGCCGGCATGAGACGGTGCAGGACTGCAATTGCTCAATCTATCCCGGCC  
ACATAACGGGTCACCGTATGGCTTGGGATATGATGATGAACTGGTACTAATAG

SEQ ID NO 15 (HCP:51)

ATGCCCGGTTGCTCTTTCTCTATCTT

SEQ ID NO 16 (HCP:52)

ATGTTGGGTAAGGTCATCGATACCCT

SEQ ID NO 17 (HCP:53)

CTATTAGGACCAGTTCATCATCATATCCCA

SEQ ID NO 18 (HCP:54)

CTATTACCAGTTCATCATCATATCCCA

SEQ ID NO 19 (HCP:107)

ATACGACGCCACGTCGATTCCCAGCTGTTCAACATC

## Fig. 21D

SEQ ID NO 20 (HCP108)

GATGGTGAACAGCTGGGAATCGACGTGGCGTCGTAT

SEQ ID NO 21 (HCC137)

ATGTTGGGTAAGGTCATCGATACCCTTACATGCGGCTTCGCCGACCTCGTGGGGTACA  
TTCCGCTCGTCGGCGCCCCCTAGGGGGCGCTGCCAGGGCCCTGGCGCATGGCGTCCG  
GGTTCTGGAGGACGGCGTGAACATATGCAACAGGGAATTTGCCCGGTTGCTCTTTCTCT  
ATCTTCCTCTTGGCTTTGCTGTCTGTCTGACCGTTCCAGCTTCCGCTTATGAAGTGCG  
CAACGTGTCCGGGATGTACCATGTACGAACGACTGCTCCAACCAAGCATTGTGTAT  
GAGGCAGCGGACATGATCATGCACACCCCCGGGTGCGTGCCCTGCGTTCCGGAGAAC  
AACTCTTCCCGCTGCTGGGTAGCGCTCACCCCCACGCTCGCAGCTAGGAACGCCAGCG  
TCCCCACCACGACAATACGACGCCACGTGATTCCCAGCTGTTACCATCTCGCCTCG  
CCGGCATGAGACGGTGCAGGACTGCAATTGCTCAATCTATCCCGGCCACATAACGGGT  
CACCGTATGGCTTGGGATATGATGATGAACTGGTCCCTACAACGGGCCCTGGTGGTAT  
CGCAGCTGCTCCGATCCACAAAGCTGTCTGTGACATGGTGGCGGGGGCCCAATTGGGG  
AGTCTGGCGGGTCTCGCCTACTATTCCATGGTGGGGAACCTGGGCTAAGGTTTTGATTG  
TGATGCTACTCTTTGCTCCCTAATAG

SEQ ID NO 23 (HCC138)

ATGTTGGGTAAGGTCATCGATACCCTTACATGCGGCTTCGCCGACCTCGTGGGGTACA  
TTCCGCTCGTCGGCGCCCCCTAGGGGGCGCTGCCAGGGCCCTGGCGCATGGCGTCCG  
GGTTCTGGAGGACGGCGTGAACATATGCAACAGGGAATTTGCCCGGTTGCTCTTTCTCT  
ATCTTCCTCTTGGCTTTGCTGTCTGTCTGACCGTTCCAGCTTCCGCTTATGAAGTGCG  
CAACGTGTCCGGGATGTACCATGTACGAACGACTGCTCCAACCAAGCATTGTGTAT  
GAGGCAGCGGACATGATCATGCACACCCCCGGGTGCGTGCCCTGCGTTCCGGAGAAC  
AACTCTTCCCGCTGCTGGGTAGCGCTCACCCCCACGCTCGCAGCTAGGAACGCCAGCG  
TCCCCACCACGACAATACGACGCCACGTGATTCCCAGCTGTTACCATCTCGCCTCG  
CCGGCATGAGACGGTGCAGGACTGCAATTGCTCAATCTATCCCGGCCACATAACGGGT  
CACCGTATGGCTTGGGATATGATGATGAACTGGTAA  
TAG

SEQ ID NO 25 (HCC139)

ATGTTGGGTAAGGTCATCGATACCCTTACATGCGGCTTCGCCGACCTCGTGGGGTACA  
TTCCGCTCGTCGGCGCCCCCTAGGGGGCGCTGCCAGGGCCCTGGCGCATGGCGTCCG  
GGTTCTGGAGGACGGCGTGAACATATGCAACAGGGAATTTGCCCGGTTGCTCTTTCTCT



100

SEQ ID NO 27 (HCC140)

[illegible]

ATGGGTAAGGTCATCGATACCCCTACGTGCGGATTCGCCGATCTCATGGGGTACATCC  
CGCTCGTCGGGCGCTCCCGTAGGAGGCGTCGCAAGAGCCCTTGCGCATGGCGTGAGGGC  
CCTTGAAGACGGGATAAAATTCGCAACAGGGAATTTGCCCGGTTGCTCCTTTTCTATTT  
TCCTTCTCGCTCTGTTCTCTTGCTTAATTCATCCAGCAGCTAGTCTAGAGTGGCGGAAT  
ACGTCTGGCCTCTATGTCCTTACCAACGACTGTTCCAATAGCAGTATTGTGTACGAGGC  
CGATGACGTTATTCTGCACACACCCGGCTGCATACCTTGTTGCCAGGACGGCAATACA  
TCCACGTGCTGGACCCCAGTGACACCTACAGTGGCAGTCAAGTACGTGCGGAGCAACCA  
CCGCTTCGATACGCAGTCATGTGGACCTATTAGTGGGCGCGGCCACGATGTGCTCTGC  
GCTCTACGTGGGTGACATGTGTGGGGCTGTCTTCCTCGTGGGACAAGCCTTCACGTTCA  
GACCTCGTCGCCATCAAACGGTCCAGACCTGTAAGTCTCGCTGTACCCAGGCCATCT  
TTCAGGACATCGAATGGCTTGGGATATGATGATGAACTGGTAATAG

Fig. 21F

SEQ ID NO 31 (HCC163)

ATGGGTAAGGTCA TCGATACCCCTAACGTGCGGATTGCGCGATCTCATGGGGTATATCC  
CGCTCGTAGGCGGGCCCCATTGGGGGCGTCGCAAGGGCTCTCGCACACGGTGTGAGGGT  
CCTTGAGGACGGGGTAAACTATGCAACAGGGAATTTACCCGGTTGCTCTTTCTCTATCT  
TTATTCTTGCTCTTCTCTCGTGTCTGACCGTTCCGGCCTCTGCAGTTCCTACCGAAATG  
CCTCTGGGATTTATCATGTTACCAATGATTGCCCAAACCTCTTCCATAGTCTATGAGGCA  
GATAACCTGATCCTACACGCACCTGGTTGCGTGCCTTGTGTGTCATGACAGGTAATGTGA  
GTAGATGCTGGGTCCAAATTACCCCTACACTGTCAGCCCCGAGCCTCGGAGCAGTCAC  
GGCTCCTCTTCGGAGAGCCGTTGACTACCTAGCGGGAGGGGGCTGCCCTCTGCTCCGGC  
TTATACGTAGGAGACGCGTGTGGGGCACTATTCTTGGTAGGCCAAATGTTACCTATA  
GGCCTCGCCAGCACGCTACGGTGCAGAACTGCAACTGTTCCATTTACAGTGGCCATGT  
TACCGGCCACCGGATGGCATGGGATATGATGATGAACTGGTAATAG

SEQ ID NO 33 (HCP109)

TGGGATATGATGATGAACTGGTC

SEQ ID NO 34 (HCP72)

CTATTATGGTGGTAAKGCCARCARGAGCAGGAG

SEQ ID NO 35 (HCC122A)

TGGGATATGATGATGAACTGGTCGCCTACAACGGCCCTGGTGGTATCGCAGCTGCTCC  
GGATCCCACAAGCTGTGCTGGACATGGTGGCGGGGGGCCCATTTGGGGAGTCTTGGCGG  
GCCTCGCCTACTATTCCATGGTGGGGAACCTGGGCTAAGGTTTTGGTTGTGATGCTACTC  
TTTGCCGGCGTCGACGGGCATACCCGCGTGTGAGGAGGGGCAGCAGCCTCCGATACCA  
GGGGCCTTGTGTCCCTCTTTAGCCCCGGGTGCGGCTCAGAAAAATCCAGCTCGTAAACAC  
CAACGGCAGTTGGCACATCAACAGGACTGCCCTGAACTGCAACGACTCCCTCCAAAC  
AGGGTTCTTTGCCGCACTATTCTACAAACACAAATTCAACTCGTCTGGATGCCAGAG  
CGCTTGGCCAGCTGTGCTCCATCGACAAGTTCGCTCAGGGGTGGGGTCCCTCACTT  
ACACTGAGCCTAACAGCTCGGACCAGAGGCCCTACTGCTGGCACTACGCGCCTCGACC  
GTGTGGTATTGTACCCGCGTCTCAGGTGTGCGGTCCAGTGATTGCTTACCCCGAGCC  
CTGTTGTGGTGGGGACGACCGATCGGTTTGGTGTCCCCACGTATAACTGGGGGGCGAA  
CGACTCGGATGTGCTGATTCTCAACAACACGCGGCCGCGGAGGCAACTGGTTCGGC  
TGTACATGGATGAATGGCACTGGGTTCCACCAAGACGTGTGGGGGGCCCCCGTGAACA  
TCGGGGGGGGCGGCAACAACACCTTGACCTGCCCCACTGACTGTTTTCGGAAGCACCC  
CGAGGCCACCTACGCCAGATGCGGTTCTGGGCCCTGGCTGACACCTAGGTGTATGGTT

Fig. 21G

CATTACCCATATAGGCTCTGGCACTACCCCTGCACTGTCAACTTCACCATCTTCAAGGT  
TAGGATGTACGTGGGGGGCGTGGAGCACAGGTTTGAAGCCGCATGCAATTGGACTCG  
AGGAGAGCGTTGTGACTTGGAGGACAGGGATAGATCAGAGCTTAGCCCCGCTGCTGCTG  
TCTACAACAGAGTGGCAGATACTGCCCTGTTCTTCACCACCCTGCCGGCCCTATCCA  
CCGGCCTGATCCACCTCCATCAGAACATCGTGGACGTGCAATACCTGTACGGTGTAGG  
GTCGGCGGTTGTCTCCCTTGTCTCATCAAATGGGAGTATGTCTGTTGCTCTTCCTTCTCT  
GGCAGACGCGCGCATCTGCGCCTGCTTATGGATGATGCTGCTGATAGCTCAAGCTGAG  
GCCGCCTTAGAGAACCTGGTGGTCTCAATGCCGCGGCCGTGGCCGGGGCGCATGGC  
ACTCTTTCTTCCTTGTGTTCTTCTGTGCTGCCTGGTACATCAAGGGCAGGCTGGTCCC  
TGGTGCGGCATACGCCTTCTATGGCGTGTGGCCGCTGCTCCTGCTTCTGCTGGCCTTAC  
CACCACGAGCTTATGCCTAGTAA

SEQ ID NO 37 (HCC141)

GATCCCACAAGCTGTCTGGACATGGTGGCGGGGGGCCATTGGGGAGTCCTGGCGGG  
CCTCGCCTACTATTCCATGGTGGGGAACTGGGCTAAGGTTTTGGTTGTGATGCTACTCT  
TTGCCGGCGTCGACGGGCATACCCGCGTGTGAGGAGGGCAGCAGCCTCCGATACCA  
GGGGCCTTGTGTCCCTCTTTAGCCCCGGGTGCGCTCAGAAAATCCAGCTCGTAAACAC  
CAACGGCAGTTGGCACATCAACAGGACTGCCCTGAACTGCAACGACTCCCTCCAAAC  
AGGGTTCTTTGCCGCACTATTCTACAAACACAAATTCAACTCGTCTGGATGCCCAGAG  
CGCTTGGCCAGCTGTGCTCCATCGACAAGTTCGCTCAGGGGTGGGGTCCCCTCACTT  
ACACTGAGCCTAACAGCTCGGACCAGAGGCCCTACTGCTGGCACTACGCGCCTCGACC  
GTGTGGTATTGTACCCGCGTCTCAGGTGTGCGGTCCAGTGTATTGCTTCACCCCGAGCC  
CTGTTGTGGTGGGGACGACCGATCGGTTTTGGTGTCCCCACGTATAACTGGGGGGCGAA  
CGACTCGGATGTGCTGATTCTCAACAACACGCGGCCGCCGCGAGGCAACTGGTTCGGC  
TGTACATGGATGAATGGCACTGGGTTACCAAGACGTGTGGGGGGCCCCCGTGCAACA  
TCGGGGGGGGCCGGCAACAACACCTTGACCTGCCCCACTGACTGTTTTCGGAAGCACCC  
CGAGGCCACCTACGCCAGATGCGGTTCTGGGCCCTGGCTGACACCTAGGTGTATGGTT  
CATTACCCATATAGGCTCTGGCACTACCCCTGCACTGTCAACTTCACCATCTTCAAGGT  
TAGGATGTACGTGGGGGGCGTGGAGCACAGGTTTGAAGCCGCATGCAATTGGACTCG  
AGGAGAGCGTTGTGACTTGGAGGACAGGGATAGATCAGAGCTTAGCCCCGCTGCTGCTG  
TCTACAACAGAGTGGCAGAGTGGCAGAGCTTAATTAATTAG

SEQ ID NO 39 (HCC142)

GATCCCACAAGCTGTCTGGACATGGTGGCGGGGGGCCATTGGGGAGTCCTGGCGGG  
CCTCGCCTACTATTCCATGGTGGGGAACTGGGCTAAGGTTTTGGTTGTGATGCTACTCT

Fig. 21H

TTGCCGGCGTCGACGGGCATACCCGCGTGTGTCAGGAGGGGCAGCAGCCTCCGATACCA  
GGGGCCTTGTGTCCCTCTTTAGCCCCGGGTGCGCTCAGAAAATCCAGCTCGTAAACAC  
CAACGGCAGTTGGCACATCAACAGGACTGCCCTGAACTGCAACGACTCCCTCCAAAC  
AGGGTTCTTTGCCGCACTATTCTACAAACACAAATTCAACTCGTCTGGATGCCCAGAG  
CGCTTGGCCAGCTGTGCTCCATCGACAAGTTCGCTCAGGGGTGGGGTCCCCTCACTT  
ACACTGAGCCTAACAGCTCGGACCAGAGGCCCTACTGCTGGCACTACGCGCCTCGACC  
GTGTGGTATTGTACCCGCGTCTCAGGTGTGCGGTCCAGTGTATTGCTTCACCCCGAGCC  
CTGTTGTGGTGGGGACGACCGATCGGTTTGGTGTCCCCACGTATAACTGGGGGGCGAA  
CGACTCGGATGTGCTGATTCTCAACAACACGCGCGCCGCGCAGGCAACTGGTTCGGC  
TGTACATGGATGAATGGCACTGGGTTTACCAAGACGTGTGGGGGGCCCCCGTGCAACA  
TCGGGGGGGGCCGGCAACAACACCTTGACCTGCCCCACTGACTGTTTTCGGAAGCACCC  
CGAGGCCACCTACGCCAGATGCGGTTCTGGGCCCTGGCTGACACCTAGGTGTATGGTT  
CATTACCCATATAGGCTCTGGCACTACCCCTGCACTGTCAACTTCACCATCTTCAAGGT  
TAGGATGTACGTGGGGGGCGTGGAGCACAGGTTTGAAGCCGCATGCAATTGGACTCG  
AGGAGAGCGTTGTGACTTGGAGGACAGGGATAGATCAGAGCTTAGCCCGCTGCTGCTG  
TCTACAACAGGTGATCGAGGGCAGACACCATCACCACCATCACTAATAG

SEQ ID NO 41 (HCC143)

ATGGTGGGGAACTGGGGCTAAGGTTTTGGTGTGATGCTACTCTTTGCCGGCGTCGACC  
GGCATACCCGCGTGTGTCAGGAGGGGCAGCAGCCTCCGATACCAGGGGCCTTGTGTCCCT  
CTTTAGCCCCGGGTGCGCTCAGAAAATCCAGCTCGTAAACACCAACGGCAGTTGGCAC  
ATCAACAGGACTGCCCTGAACTGCAACGACTCCCTCCAAACAGGGTTCTTTGCCGCA  
TATTCTACAAACACAAATTCAACTCGTCTGGATGCCCAGAGCGCTTGGCCAGCTGTG  
CTCCATCGACAAGTTCGCTCAGGGGTGGGGTCCCCTCACTTACACTGAGCCTAACAGC  
TCGGACCAGAGGCCCTACTGCTGGCACTACGCGCCTCGACCGTGTGGTATTGTACCCG  
CGTCTCAGGTGTGCGGTCCAGTGTATTGCTTCACCCCGAGCCCTGTTGTGGTGGGGAC  
GACCGATCGGTTTGGTGTCCCCACGTATAACTGGGGGGCGAACGACTCGGATGTGCTG  
ATTCTCAACAACACGCGCGCCGCGCAGGCAACTGGTTCGGCTGTACATGGATGAATG  
GCACTGGGTTTACCAAGACGTGTGGGGGGCCCCCGTGCAACATCGGGGGGGCCGGCA  
ACAACACCTTGACCTGCCCCACTGACTGTTTTCGGAAGCACCCCGAGGCCACCTACGC  
CAGATGCGGTTCTGGGCCCTGGCTGACACCTAGGTGTATGGTTTATTACCCATATAGG  
CTCTGGCACTACCCCTGCACTGTCAACTTCACCATCTTCAAGGTTAGGATGTACGTGG  
GGGCGTGGAGCACAGGTTTGAAGCCGCATGCAATTGGACTCGAGGAGAGCGTTGTGA  
CTTGGAGGACAGGGATAGATCAGAGCTTAGCCCGCTGCTGCTGTCTACAACAGAGTGG  
CAGAGCTTAATTAATTAG

Fig. 21I

SEQ ID NO 43 (HCCI44)

ATGGTGGGGAAC TGGGCTAAGGTTTTGGTTGTGATGCTACTCTTTGCCGGCGTCGACG  
GGCATACCCGCGTGT CAGGAGGGGCAGCAGCCTCCGATACCAGGGGCCTTGTGTCCCT  
CTTTAGCCCCGGGT CGGCTCAGAAAATCCAGCTCGTAAACACCAACGGCAGTTGGCAC  
ATCAACAGGACTGCCCTGAACTGCAACGACTCCCTCCAAACAGGGTTCTTTGCCGCAC  
TATTCTACAAACACAAATTCAACTCGTCTGGATGCCCGAGAGCGCTTGGCCAGCTGTCTG  
CTCCATCGACAAGTTCGCTCAGGGGTGGGGTCCCTCACTTACACTGAGCCTAACAGC  
TCGGACCAGAGGCCCTACTGCTGGCACTACGCGCCTCGACCGTGTGGTATTGTACCCG  
CGTCTCAGGTGTGCGGTCCAGTGTAATTGCTTCACCCCGAGCCCTGTTGTGGTGGGGAC  
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CAGATGCGGTTCTGGGCCCTGGCTGACACCTAGGTGTATGGTTCATTACCCATATAGG  
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SEQ ID NO 45 (HCCL64)

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Fig. 21J

TGGAGCACAGGTTCCAAGCCGCATGCAATTGGA CTGAGGAGAGCGTTGTGACTTGGA  
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SEQ ID NO 47 (HCC165)

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CAACGTGTCCGGGATGTACCATGTACGAACGACTGCTCCAACTCAAGCATTGTGTAT  
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CCATCTCGCCTCGCCGGCATGAGACGGTGCAGGACTGCAATTGCTCAATCTATCCCGG  
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Fig. 21K

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CGAAGCCGCATGCAATTGGACTCGAGGAGAGCGTTGTGACTTGGAGGACAGGGATAG  
ATCAGAGCTTAGCCCGCTGCTGCTGTCTACAACAGAGTGGCAGATACTGCCCTGTTCC  
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TGATGCTGCTGATAGCTCAAGCTGAGGCCGCTTAGAGAACCTGGTGGTCTCAATGC  
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SEQ ID NO 49 (HCC168)

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GTCAGGAGGGGCAGCAGCCTCCGATACCAGGGGCCTTGTGTCCCTCTTTAGCCCCGGG

Fig. 21L

TCGGCTCAGAAAATCCAGCTCGTAAACACCAACGGCAGTTGGCACATCAACAGGACT  
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GGGATAGATCAGAGCTTAGCCCGCTGCTGCTGTCTACAACAGAGTGGCAGATACTGCC  
CTGTTCCCTTCACCAACCCCTGCCGGCCCTATCCACCGGCCTGATCCACCTCCATCAGAAC  
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GCTGCCTGGTACATCAAGGGCAGGCTGGTCCCTGGTGCGGCATACGCCTTCTATGGCG  
TGTGGCCGCTGCTCCTGCTTCTGCTGGCCTTACCACCACGAGCTTATGCCTAGTAA



Fraction	volume	dilution	39 Type 1b	40 Type 1b	62 Type 3a	63 Type 5a
START	23 ml	1/20	2.517	1.954	1.426	1.142
FLOW THROUGH	23 ml	1/20	0.087	0.085	0.176	0.120
1	0.4 ml	1/200	0.102	0.051	0.048	0.050
2			0.396	0.550	0.090	0.067
3			2.627	2.603	2.481	2.372
4			3	2.967	3	2.694
5			3	2.810	2.640	2.154
6			2.694	2.499	1.359	1.561
7			2.408	2.481	0.347	1.390
8			2.176	1.970	1.624	0.865
9			1.461	1.422	0.887	0.604
10			1.236	0.926	0.543	0.519
11			0.981	0.781	0.294	0.294
12			0.812	0.650	0.249	0.199
13			0.373	0.432	0.239	0.209
14			0.653	0.371	0.145	0.184
15			0.441	0.348	0.151	0.151
16			0.321	0.374	0.098	0.106
17			0.525	0.186	0.099	0.108
18			0.351	0.171	0.083	0.090
19			0.192	0.164	0.084	0.087

1. *Chlorophyll a* and *Chlorophyll b* were determined by the method of Arar and Collins (1971). The concentration of chlorophylls was expressed in  $\mu\text{g mL}^{-1}$  of the sample.

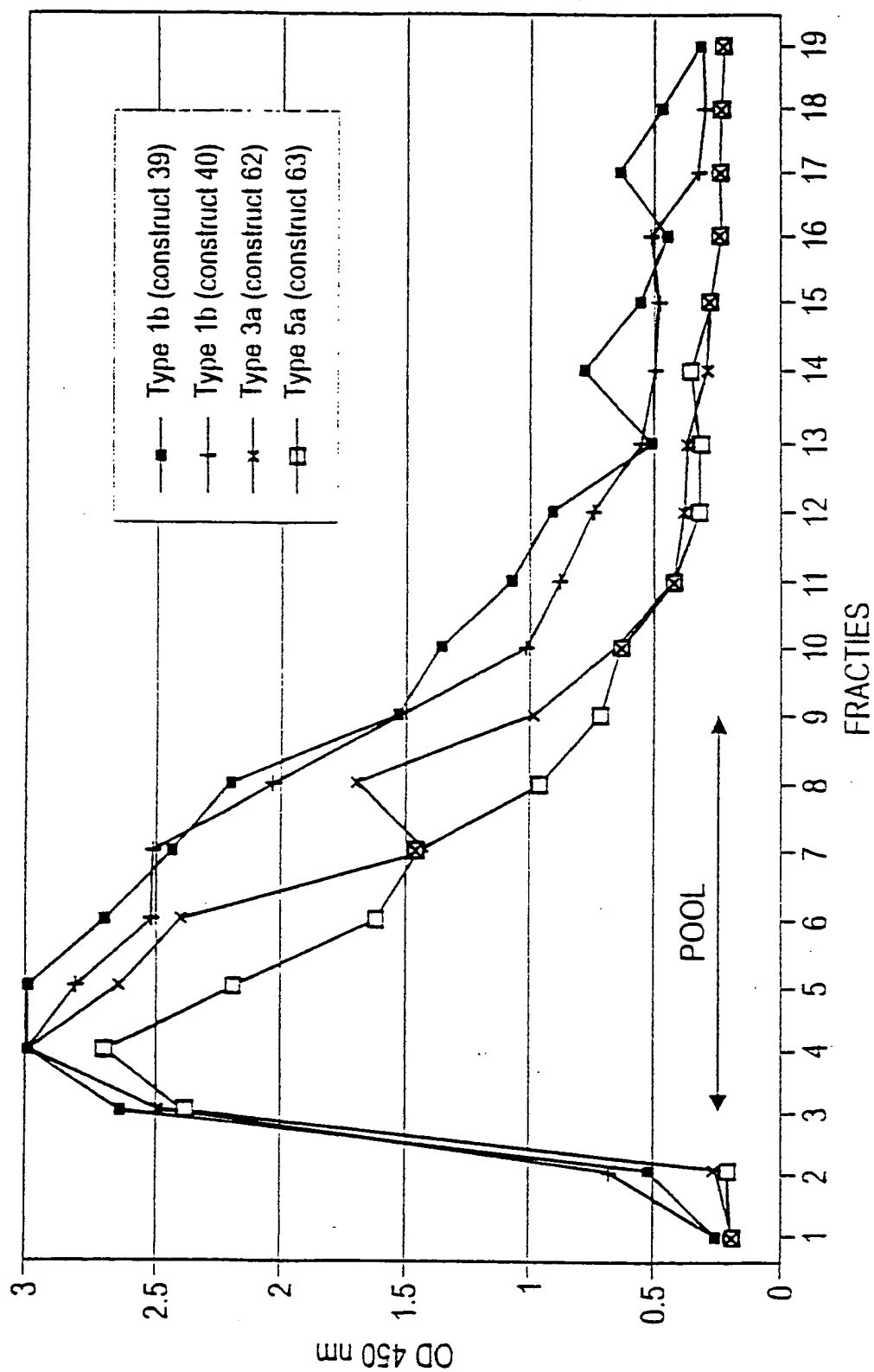


Fig. 23

Figure 24

Fraction	volume	dilution	OD measured at 450 nm			
			construct			
			39 Type 1b	40 Type 1b	62 Type 3a	63 Type 5a
20	250 $\mu$ l	1/200	0.072	0.130	0.096	0.051
21			0.109	0.293	0.084	0.052
22			0.279	0.249	0.172	0.052
23			0.093	0.151	0.297	0.054
24			0.080	0.266	0.438	0.056
25			0.251	0.100	0.457	0.048
26			3	1.649	0.722	0.066
27			3	3	2.526	0.389
28			3	3	3	2.345
29			3	3	2.349	2.580
30			2.227	1.921	1.424	1.333
31			0.263	0.415	0.356	0.162
32			0.071	0.172	0.154	0.064
33			0.103	0.054	0.096	0.057
34			0.045	0.045	0.044	0.051
35			0.043	0.047	0.045	0.046
36			0.045	0.045	0.049	0.040
37			0.045	0.047	0.046	0.048
38			0.046	0.048	0.047	0.057
39			0.045	0.048	0.050	0.057
40			0.046	0.049	0.048	0.049

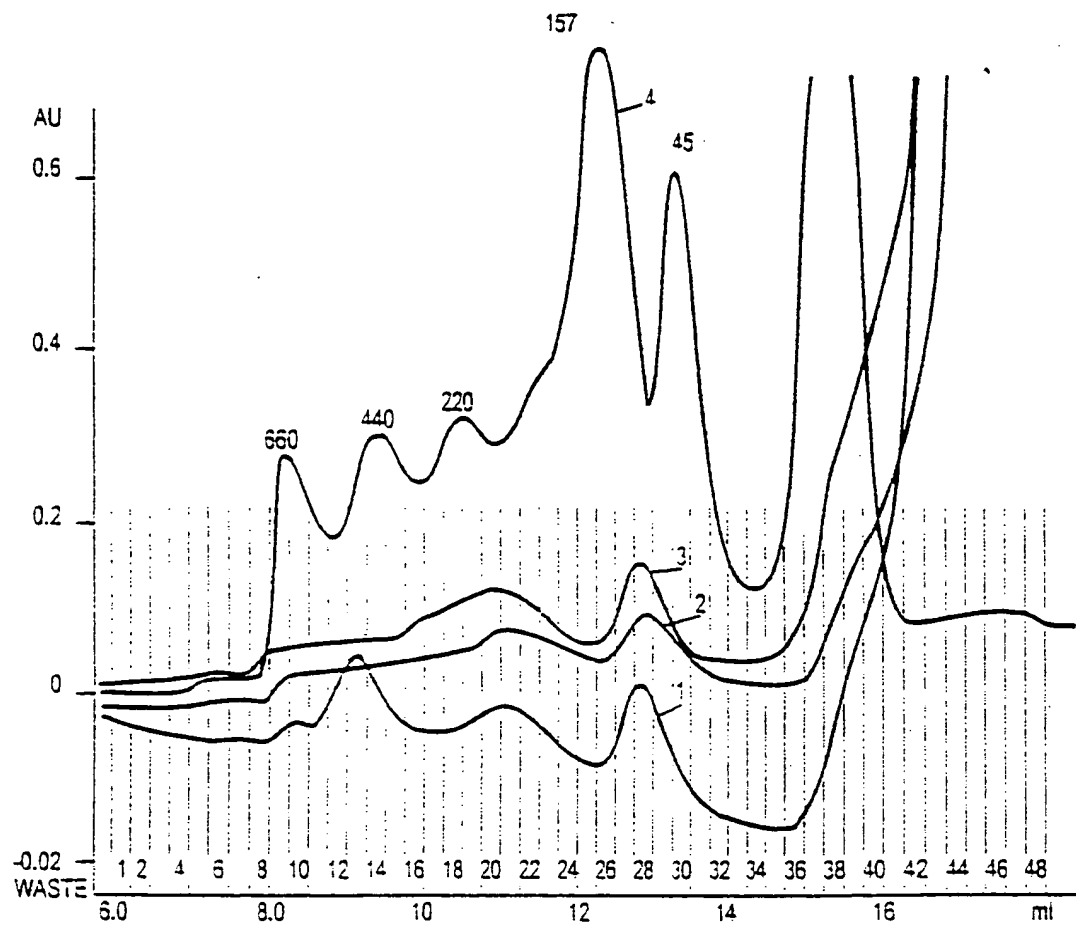


Fig. 25

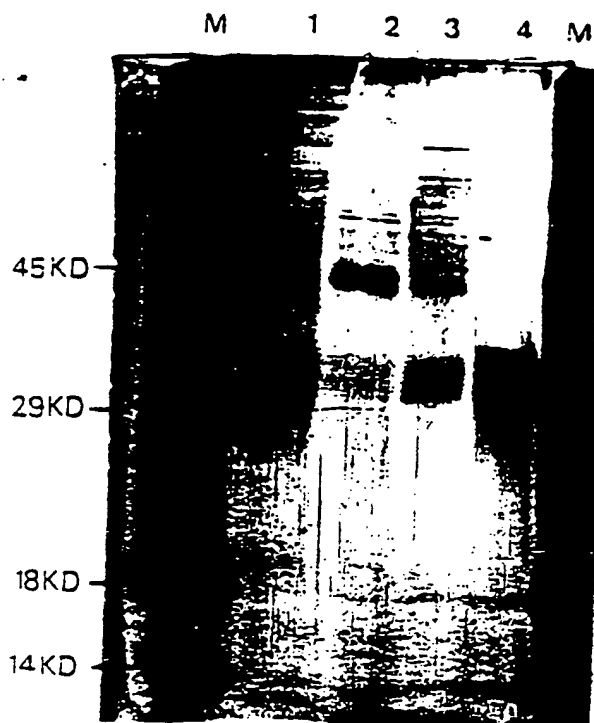


Fig. 26

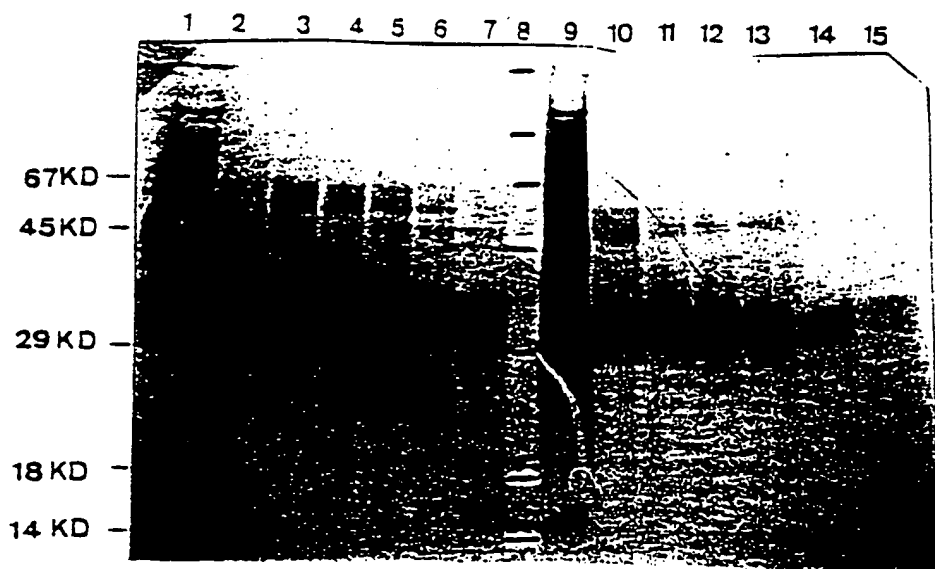


Fig. 27

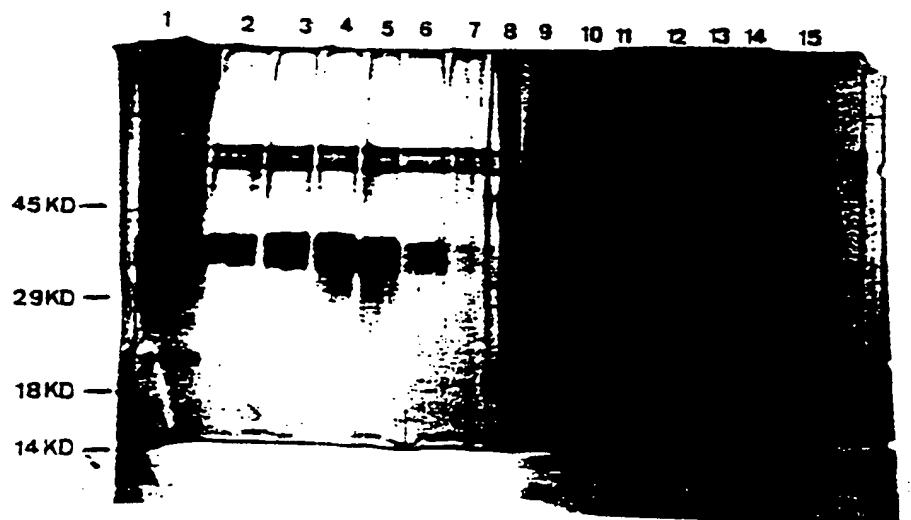


Fig.28

M 1 2 3 4 5 6

67 kD -

45 kD -

29 kD -

18 kD -

14 kD -

Fig.29

Lane 1: Crude Lysate  
 Lane 2: Flow through Lentil Chromatography  
 Lane 3: Wash with EMPIGEN Lentil Chromatography  
 Lane 4: Eluate Lentil Chromatography  
 Lane 5: Flow through during concentration lentil eluate  
 Lane 6: Pool of E1 after Size Exclusion Chromatography

00006794-13004

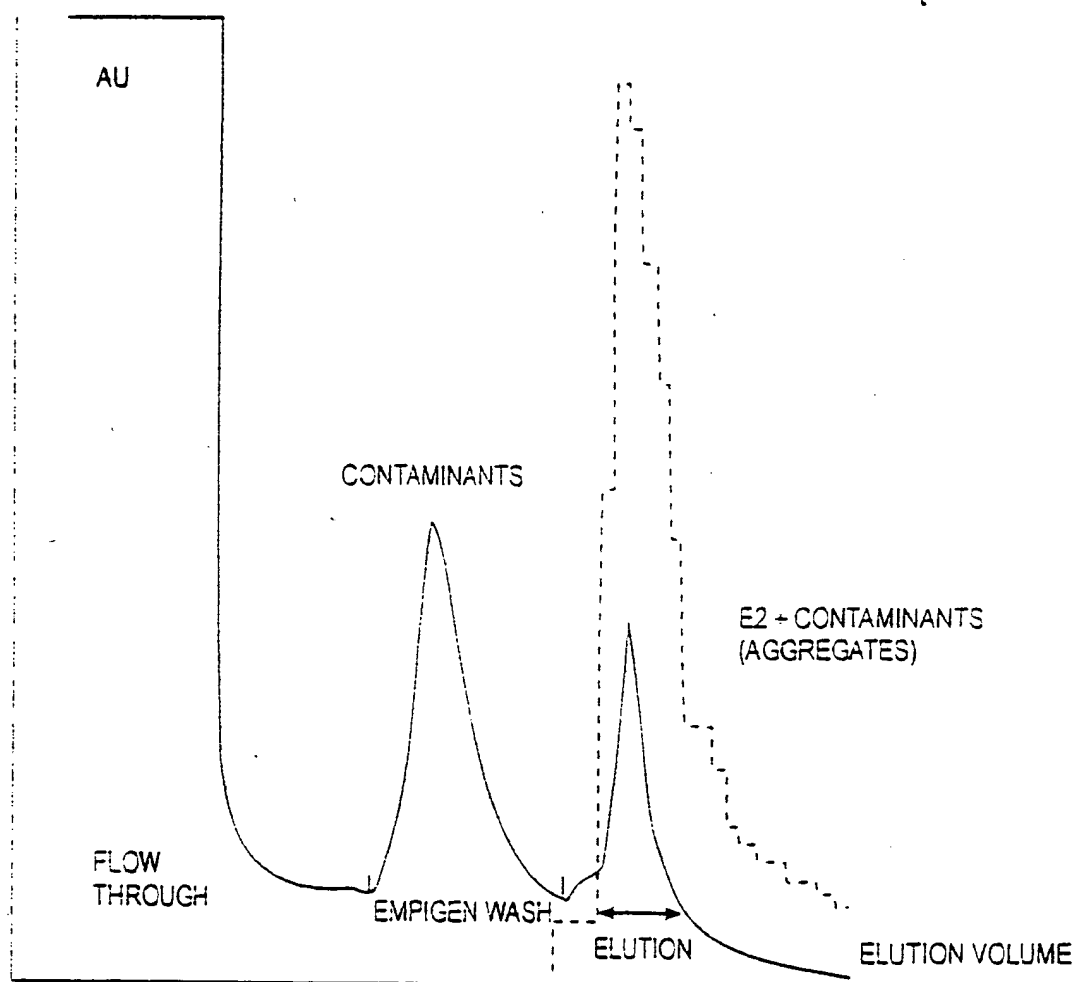
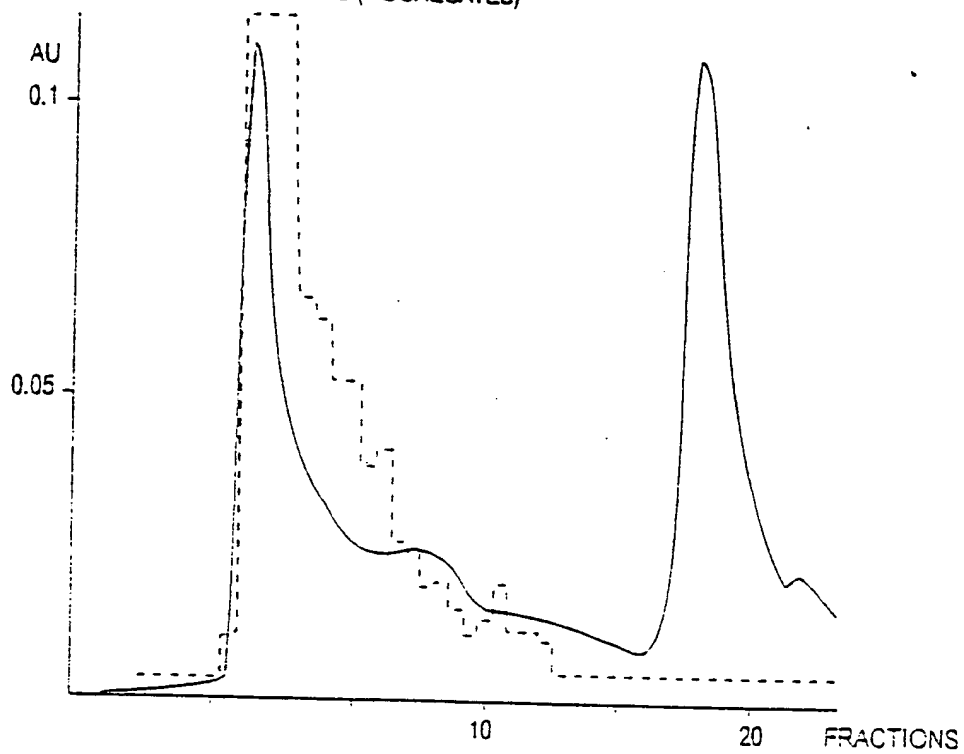


Fig. 30

NON - REDUCED

Fig. 31A

E2 + CONTAMINANTS (AGGREGATES)



REDUCED

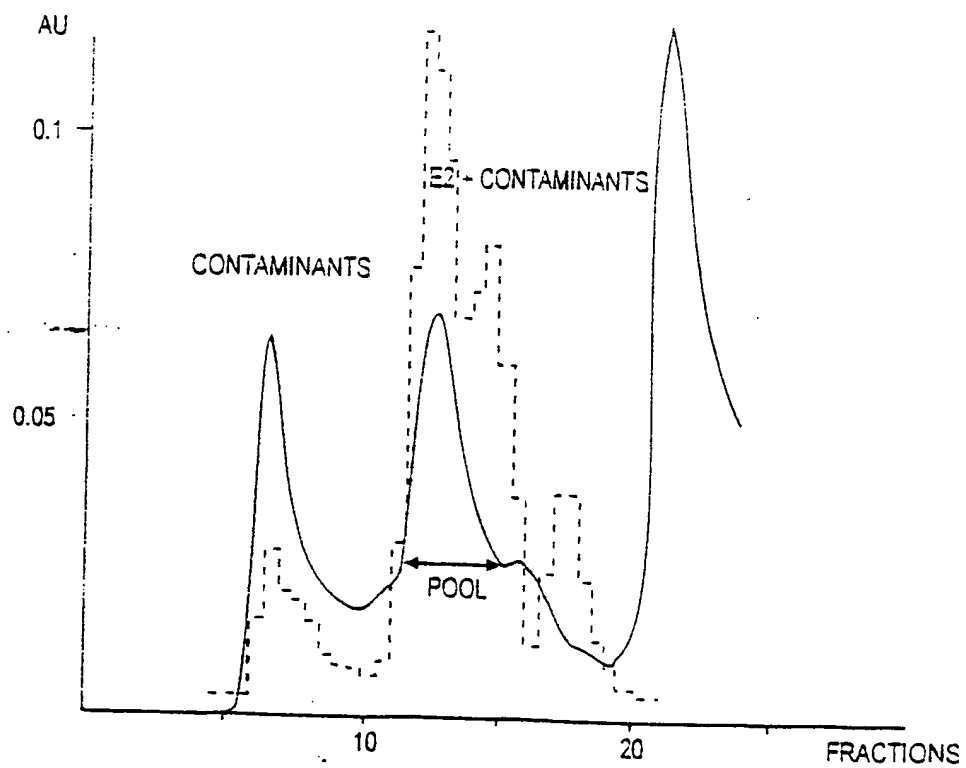


Fig. 31B



FIG. 32

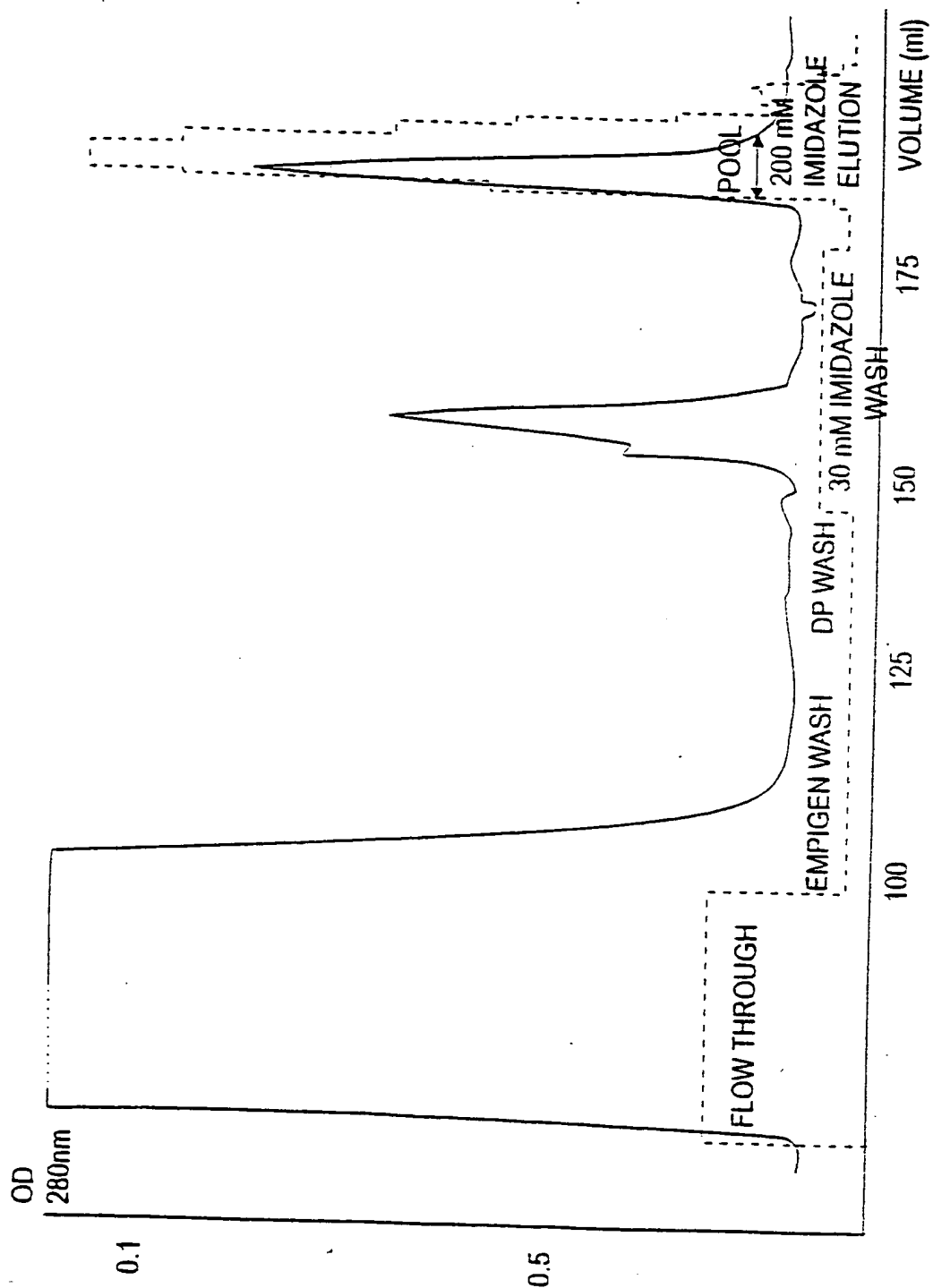
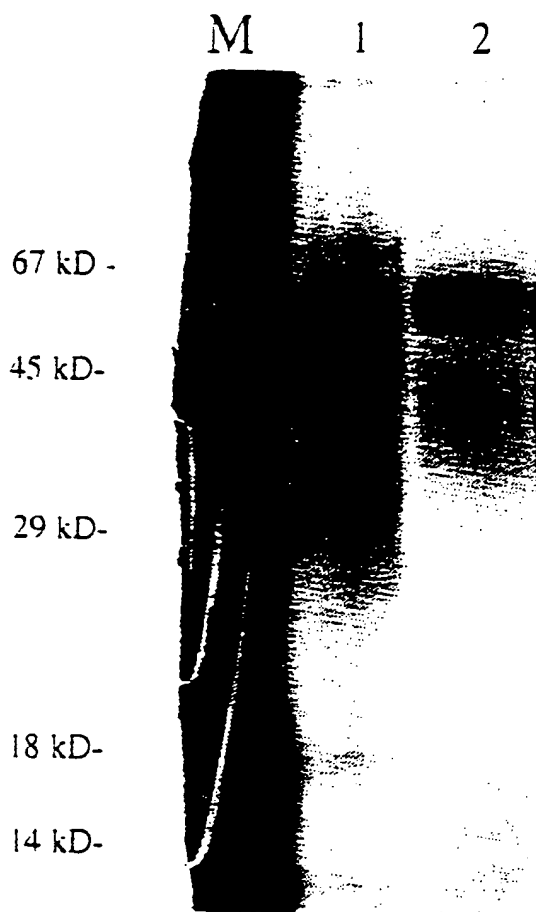


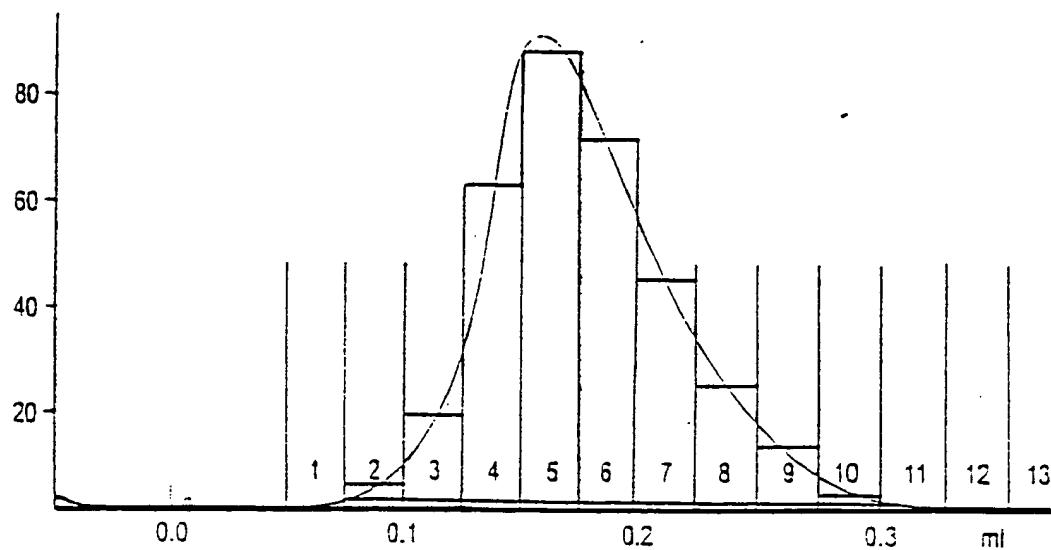
Fig. 32

# SILVER STAIN OF PURIFIED E2



1. 30 mM IMIDAZOLE WASH Ni-IMAC
2. 0.5 ug E2

Fig.33



No.	Ret. (ml)	Peak start (ml)	Peak end (ml)	Dur (ml)	Area (ml* $\mu$ AU)	Height ( $\mu$ AU)
1	-0.45	-0.46	-0.43	0.04	0.0976	4.579
2	1.55	0.73	3.26	2.51	796.4167	889.377
3	3.27	3.26	3.31	0.05	0.0067	0.224
4	3.35	3.32	3.35	0.02	0.0002	0.018

Total number of detected peaks = 4  
 Total Area above baseline = 0.796522 ml\*AU  
 Total area in evaluated peaks = 0.796521 ml\*AU  
 Ratio peak area / total area = 0.999999  
 Total peak duration = 2.613583 ml

Fig. 34

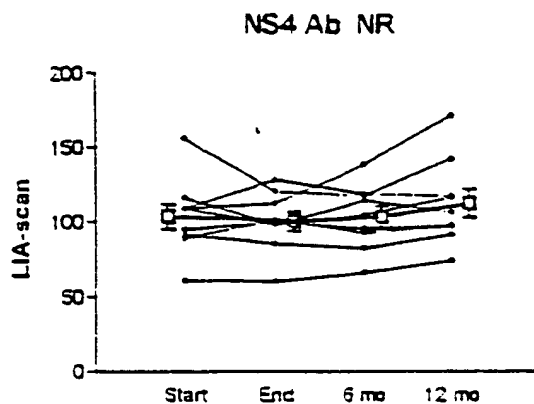


Fig. 35A-1

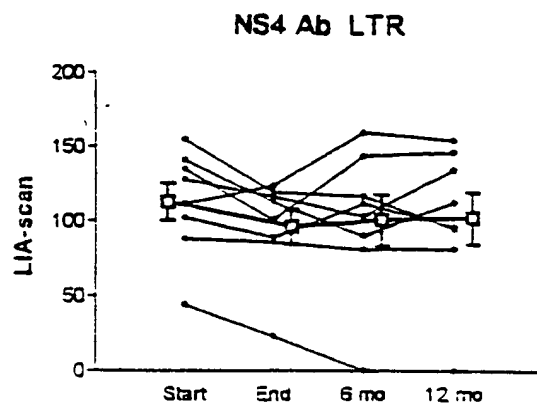


Fig. 35A-2

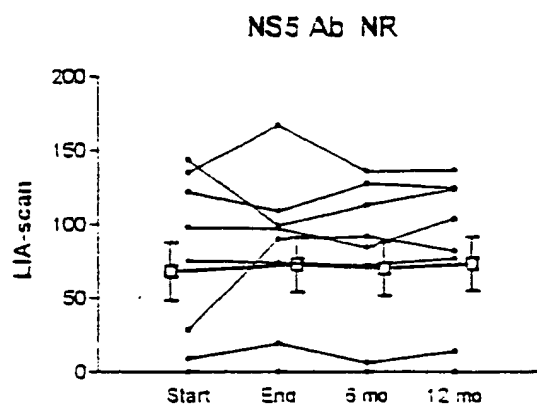


Fig. 35A-3

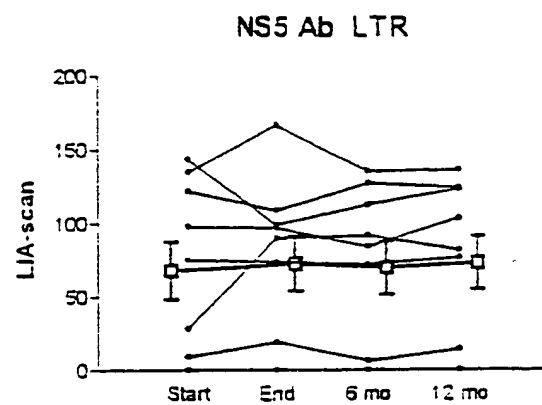


Fig. 35A-4

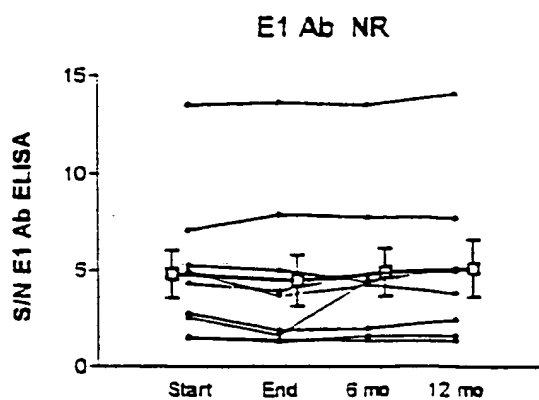


Fig. 35A-5

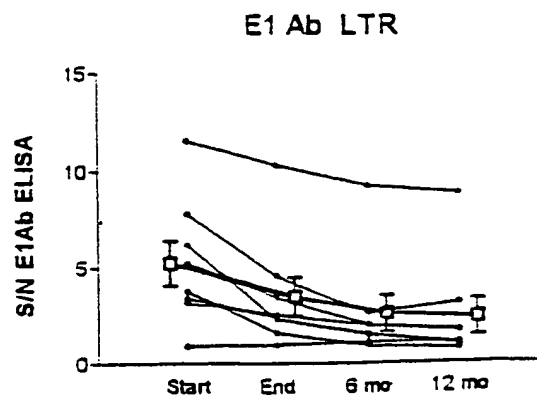
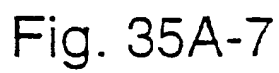


Fig. 35A-6

[illegible]

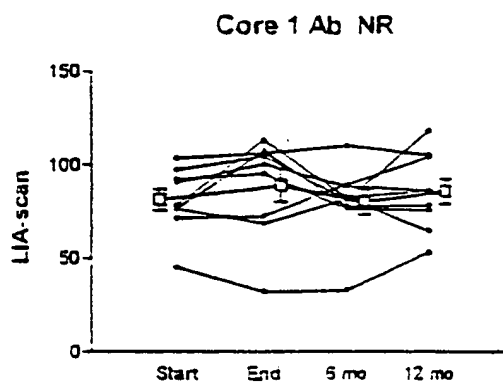


Fig. 35B-1

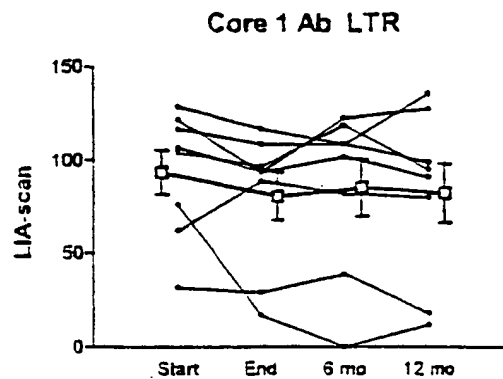


Fig. 35B-2

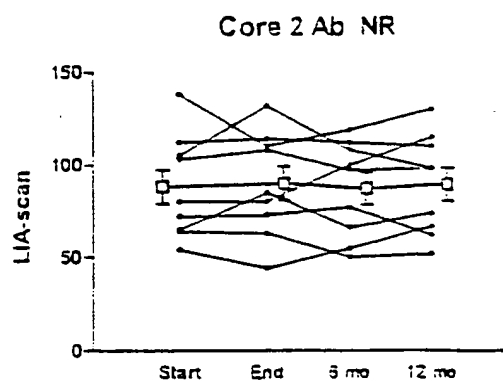


Fig. 35B-3

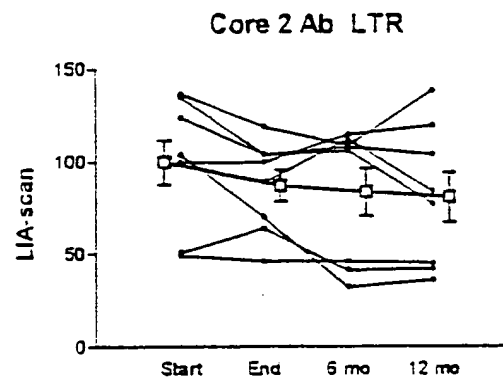


Fig. 35B-4

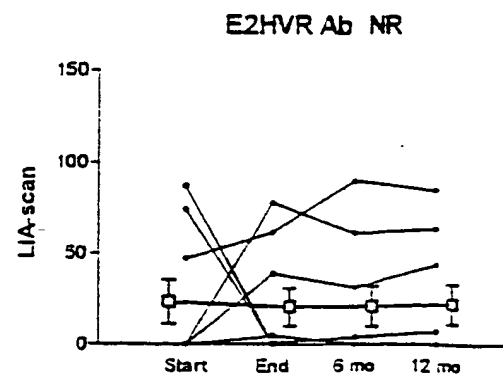


Fig. 35B-5

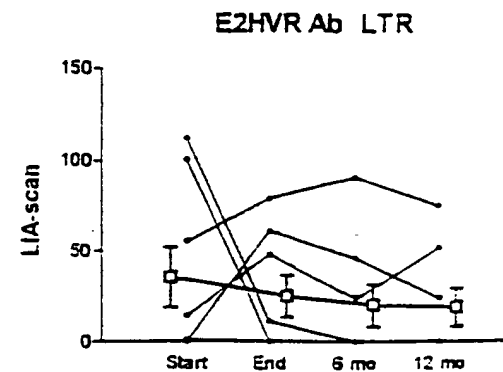


Fig. 35B-6

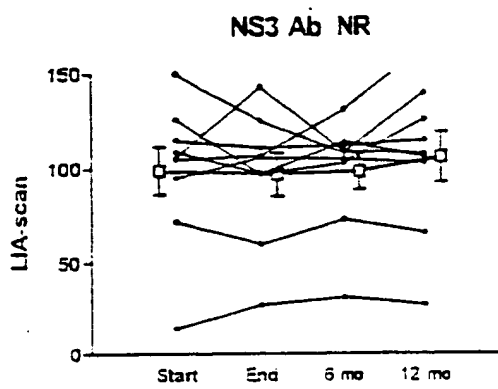


Fig. 35B-7

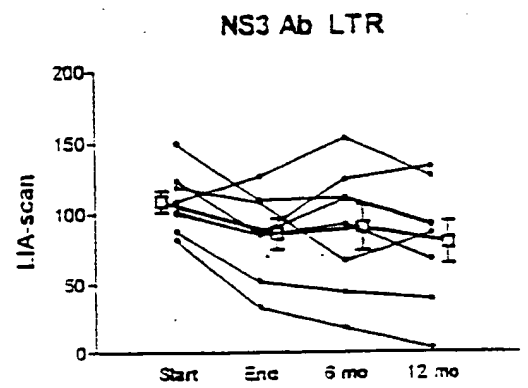


Fig. 35B-8

Fig. 36A

E1 Ab

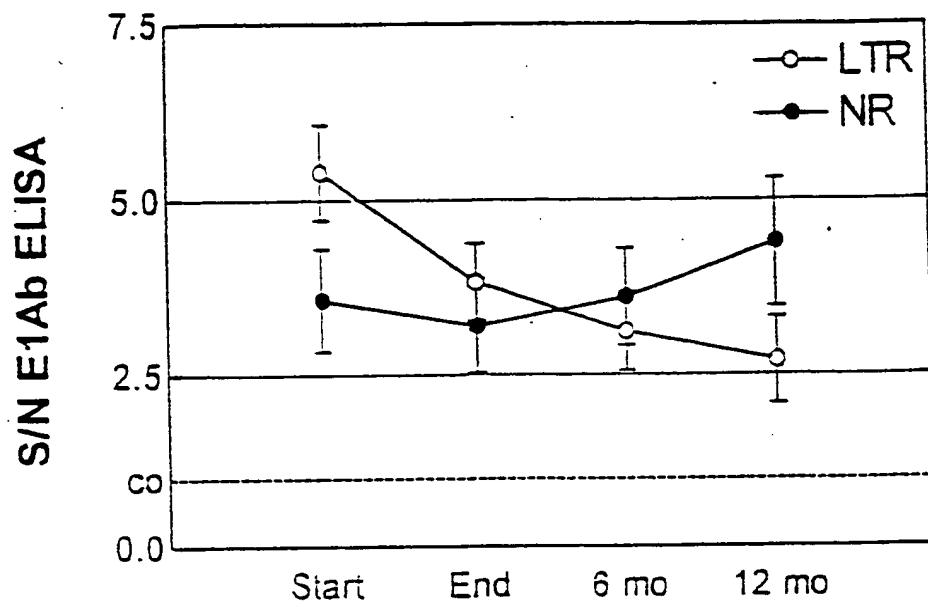


Fig. 36B

E2 Ab

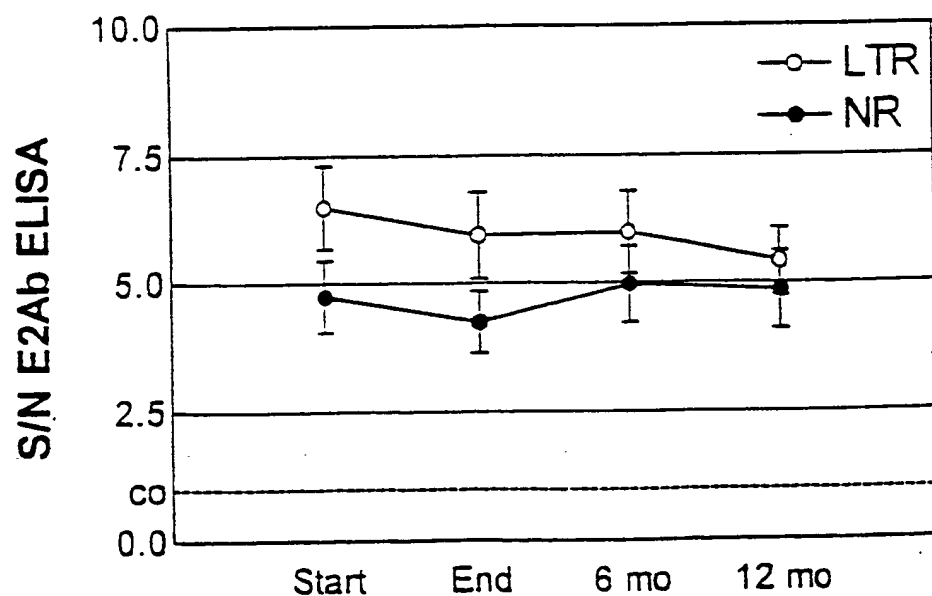




Fig. 37A

Non Responders

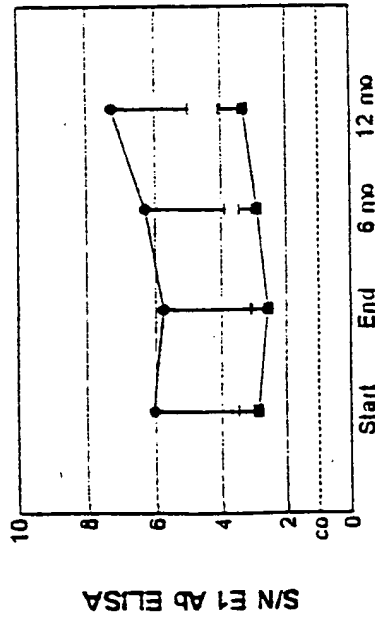


Fig. 37C

Type 1b

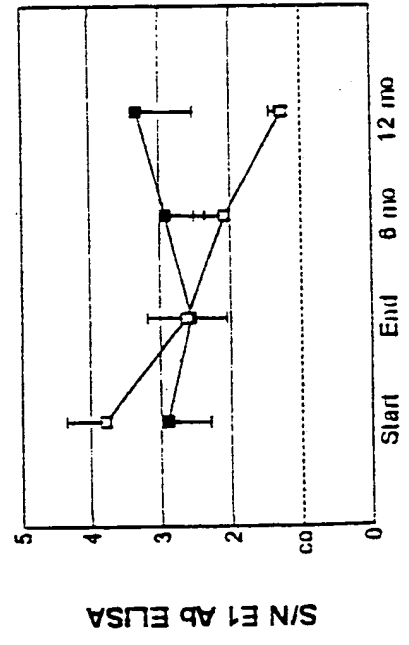


Fig. 37B

Long Term Responders

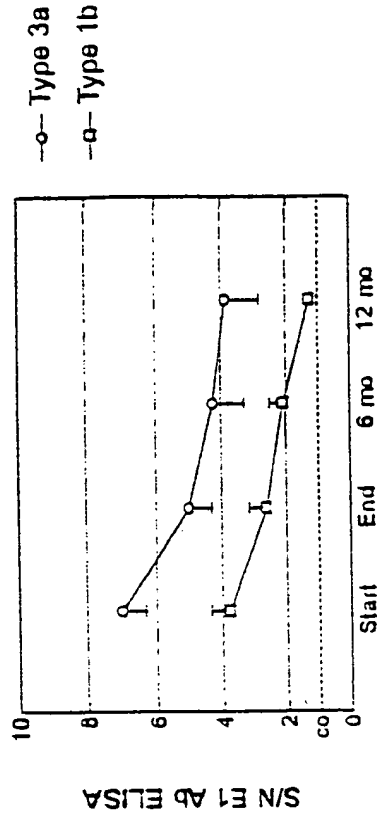


Fig. 37D

Type 3a

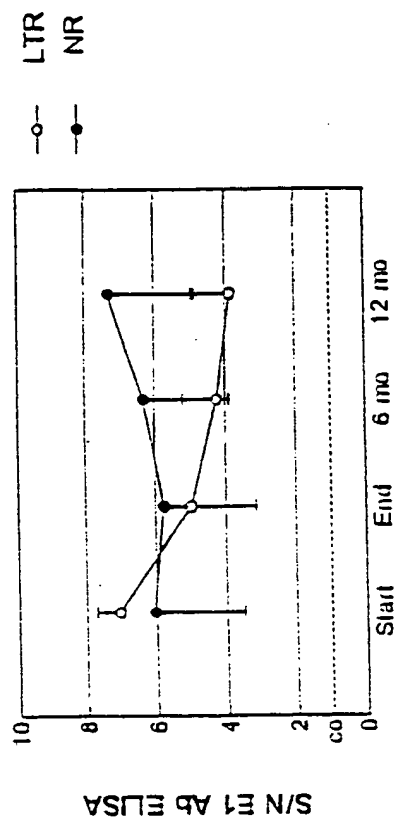
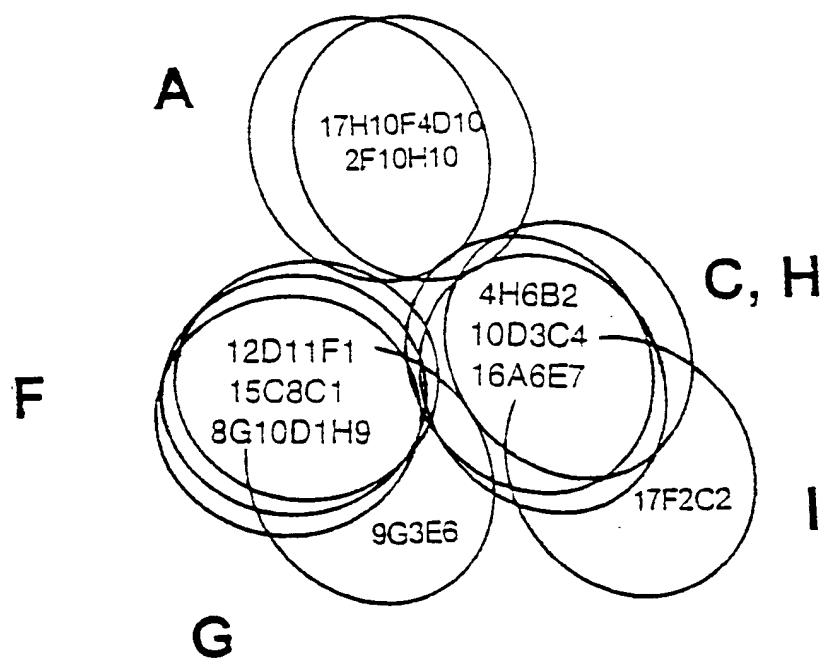


Fig. 38

Relative Map Positions of  
anti-E2 monoclonal antibodies





# PARTIAL TREATMENT OF HCV E2\ E2s ENVELOPE PROTEINS BY PNGase F

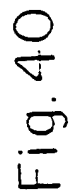


Fig. 41 *In Vitro* Mutagenesis of HCV E1 glycoprotein

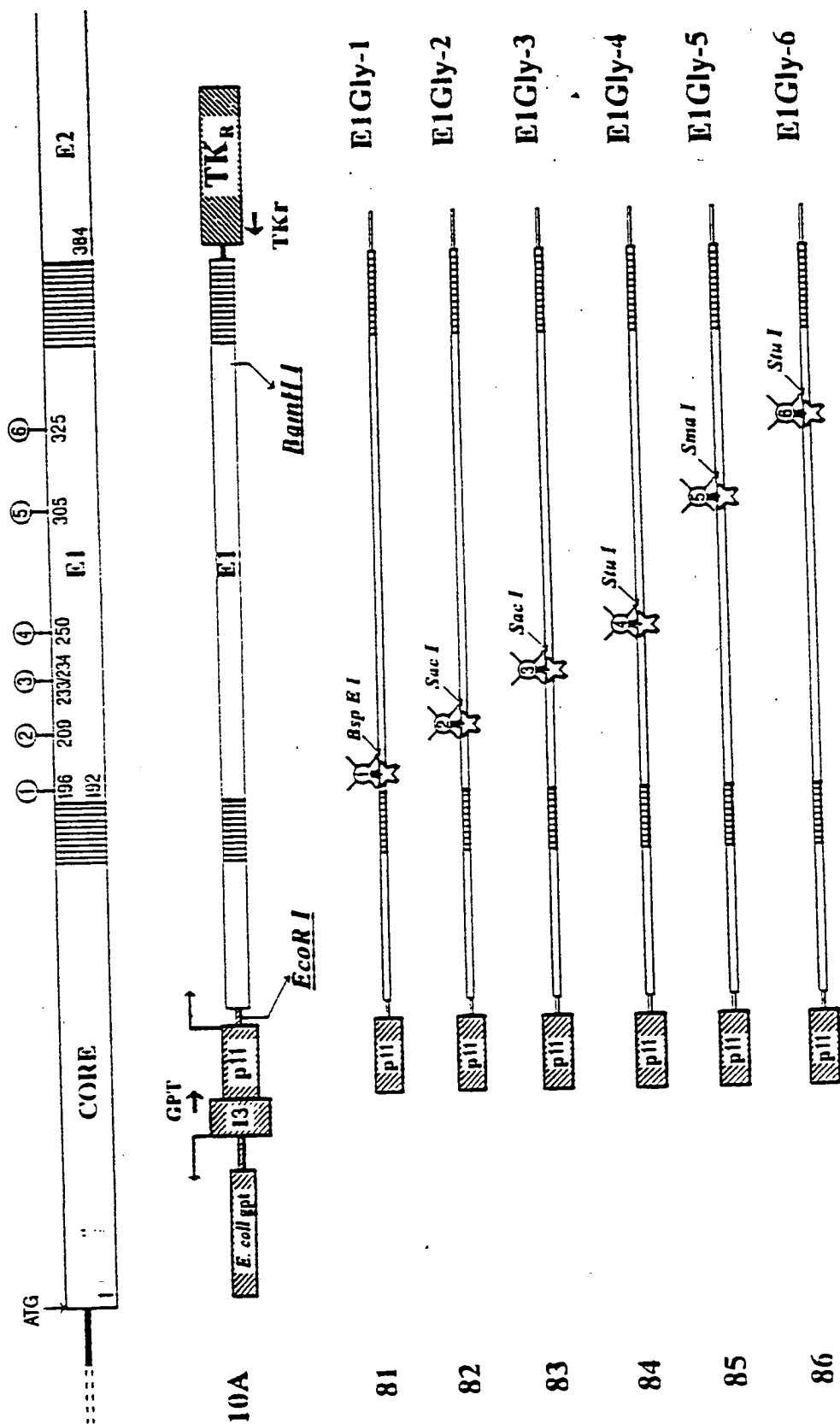
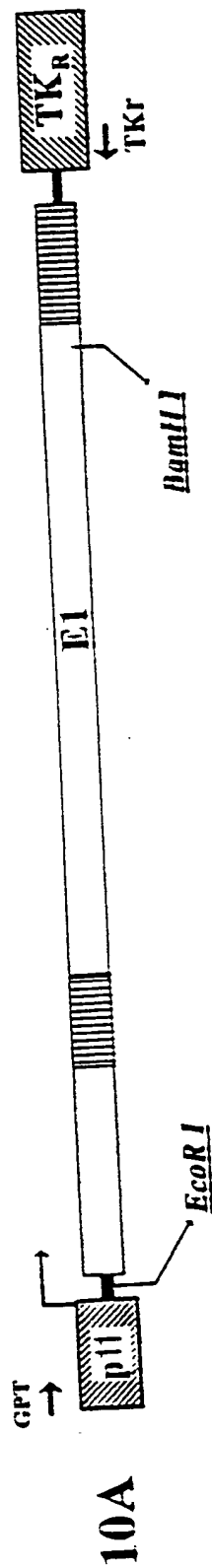
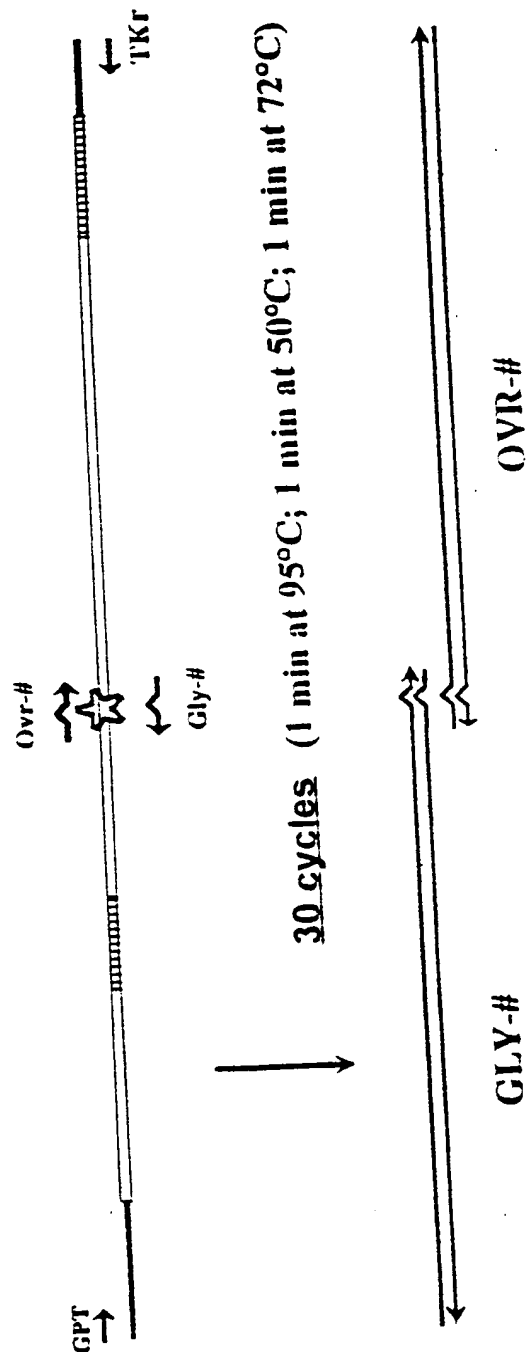


Fig. 42A *In Vitro* Mutagenesis of HCV E1 glycoprotein



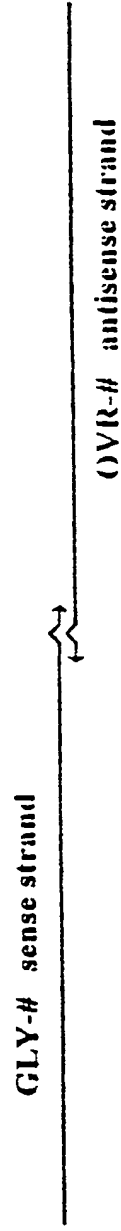
1. First step of PCR amplification (Gly-# and Ovr-# primers)



## 2. Overlap extension and nested PCR

Fig. 42B

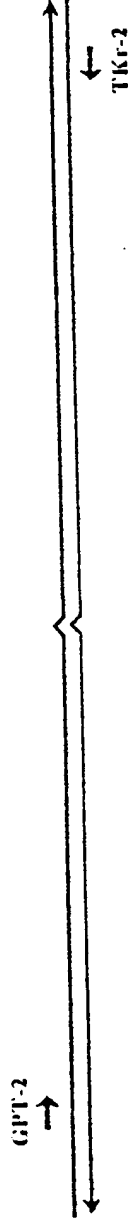
### a. Overlap extension



↓  
2 cycles (1 min at 95°C; 1 min at 50°C; 1 min at 72°C)



### b. Nested PCR amplification (GPI-2 and TKR-2 primers)



↓  
25 cycles (1 min at 95°C; 1 min at 55°C; 1 min at 72°C)

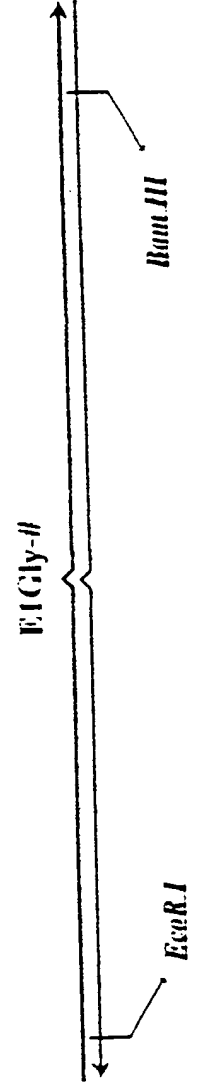
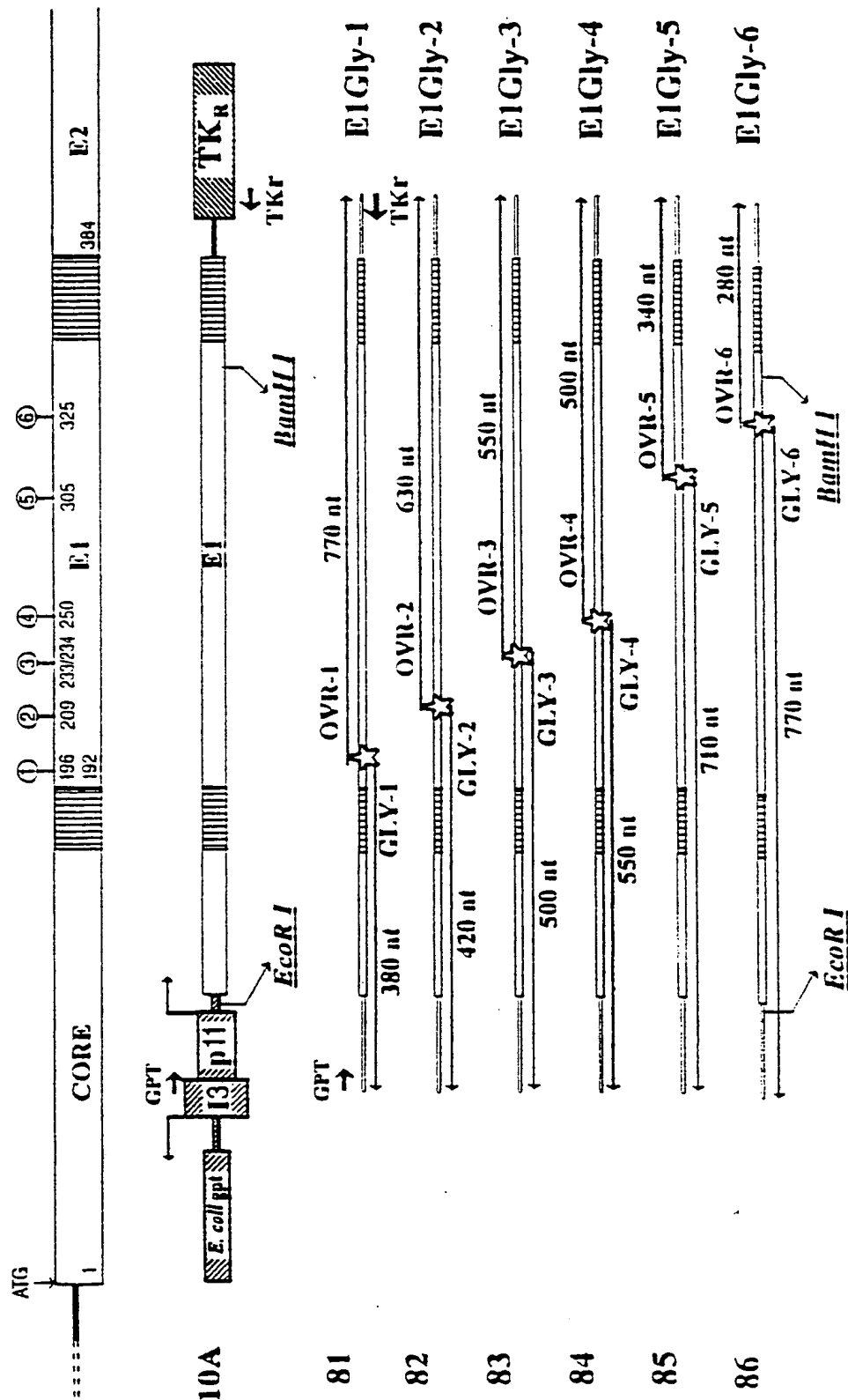


Fig. 43 *In Vitro* Mutagenesis of HCV E1 glycoprotein





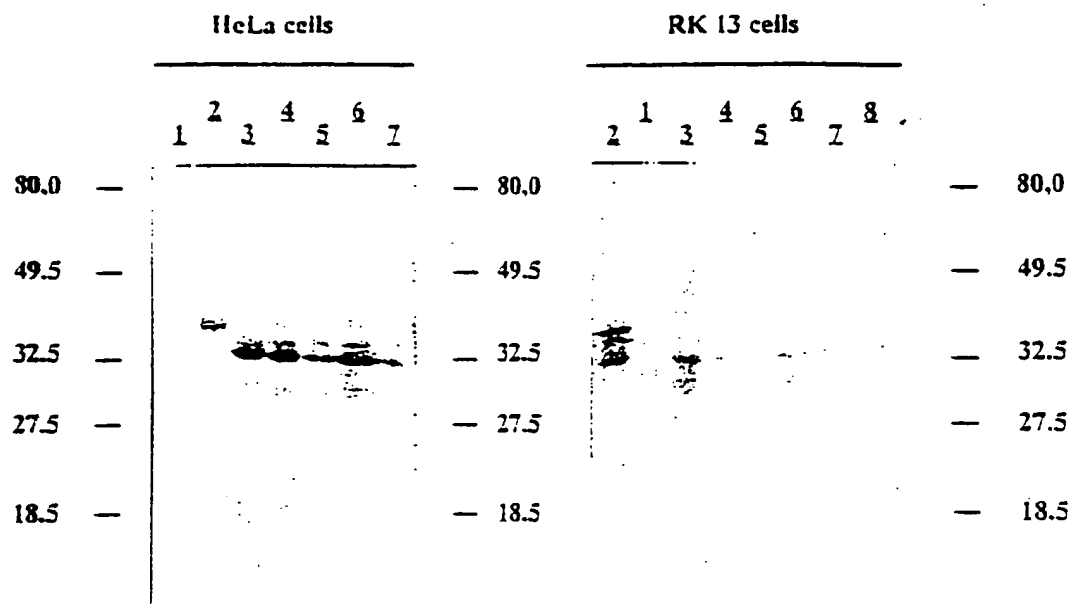


Fig. 44A

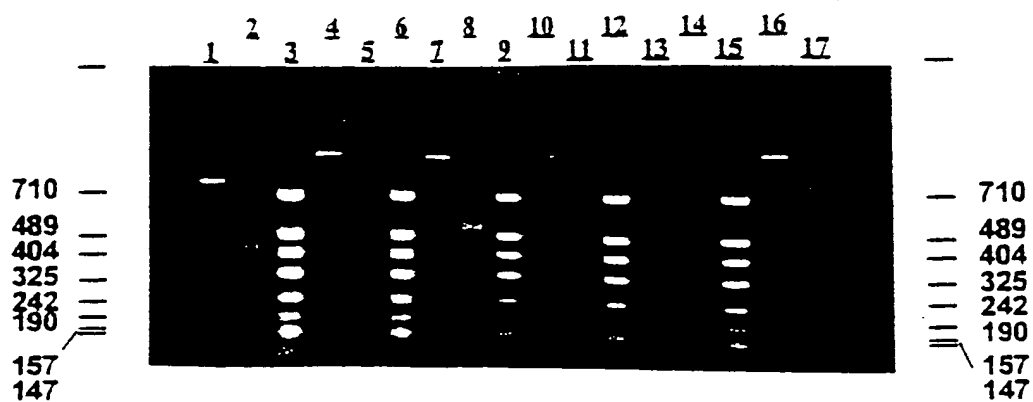


Fig. 44B

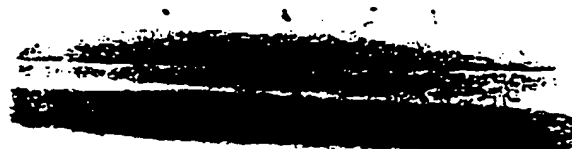


Fig.45

KDa 119 67 43 29 18

| | | | |



Fig.46

Fig. 47

	age (years)	HCV infection (years)	genotype
Marcel	17	9	1a
Peggy	21	16.5	1b
Fenna	15	9	1a
Yoran	12	none	
Marti	12	none	

chronic carriers (strong T-cell adjuvant)

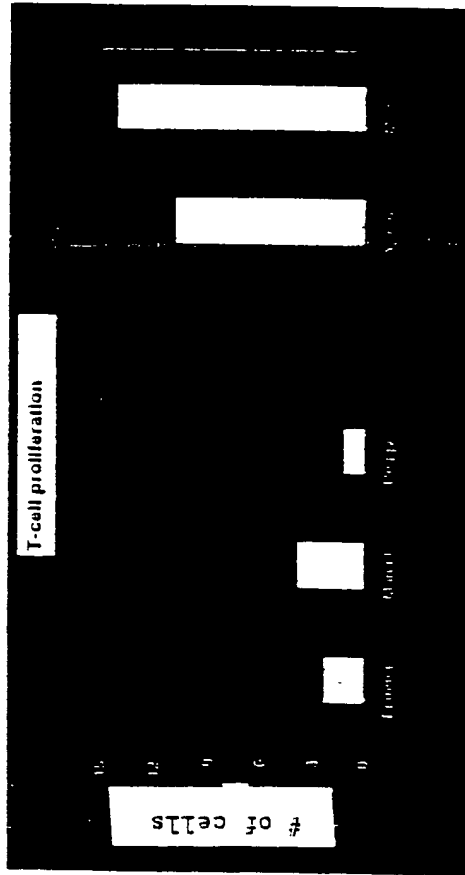
↓ ↓ ↓ ↓ ↓ ↓      ↓ ↓ ↓ ↓ ↓ ↓ 50 µg E1 dose  
 0 3 6 9 12 15      26 29 32 35 38 41 weeks

naive (alum)

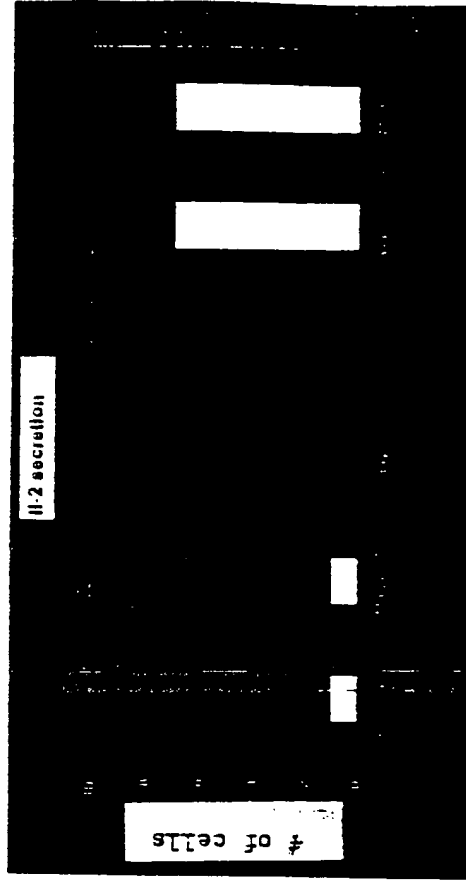
↓ ↓ ↓ ↓ ↓ ↓      50 µg E1 dose  
 0 3 6 9 12 15 weeks

**Fig. 48**

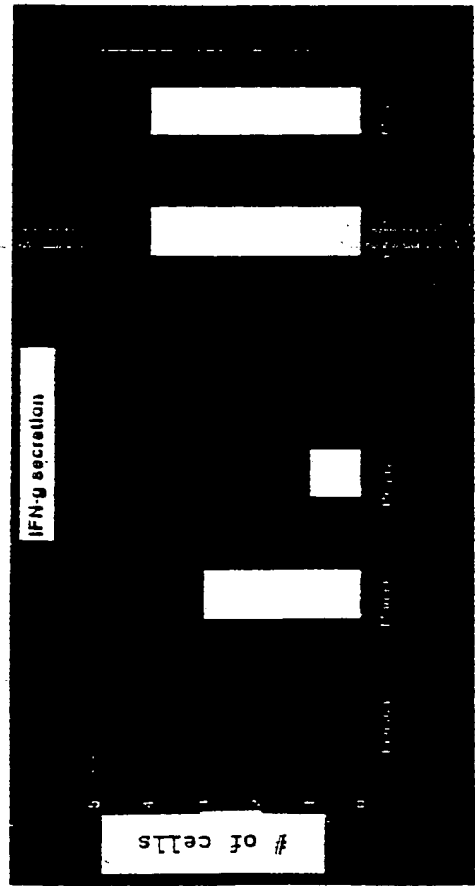
48a



48b



48c



48d

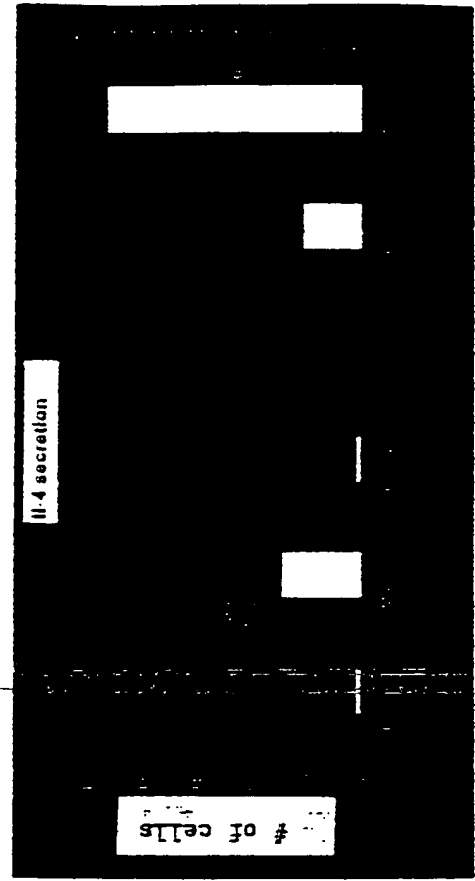
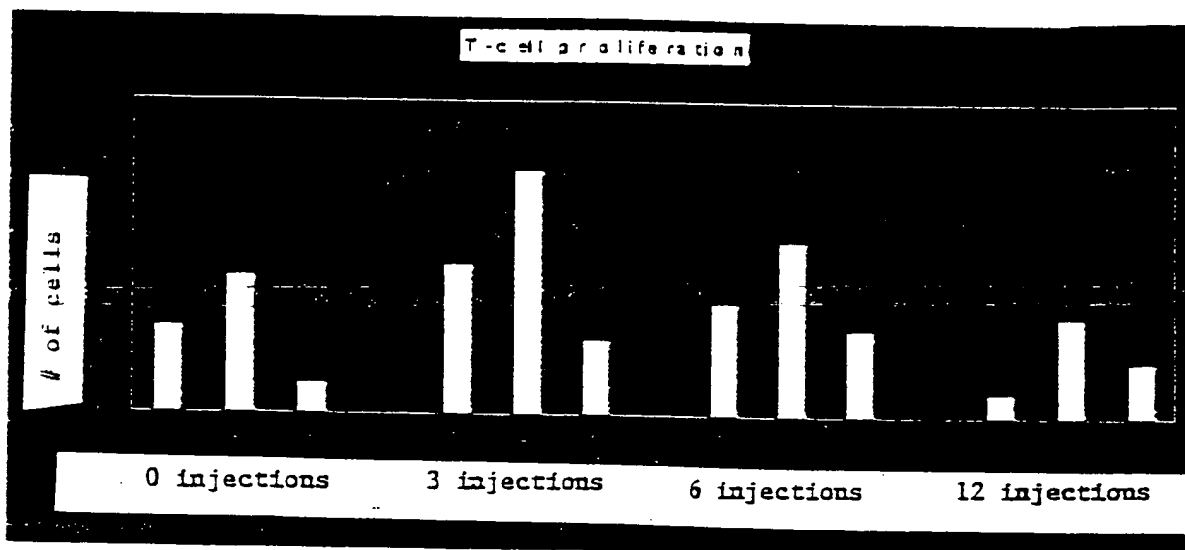


Fig. 49



1 Fem m a, 2 Marcel, 3 Peggy

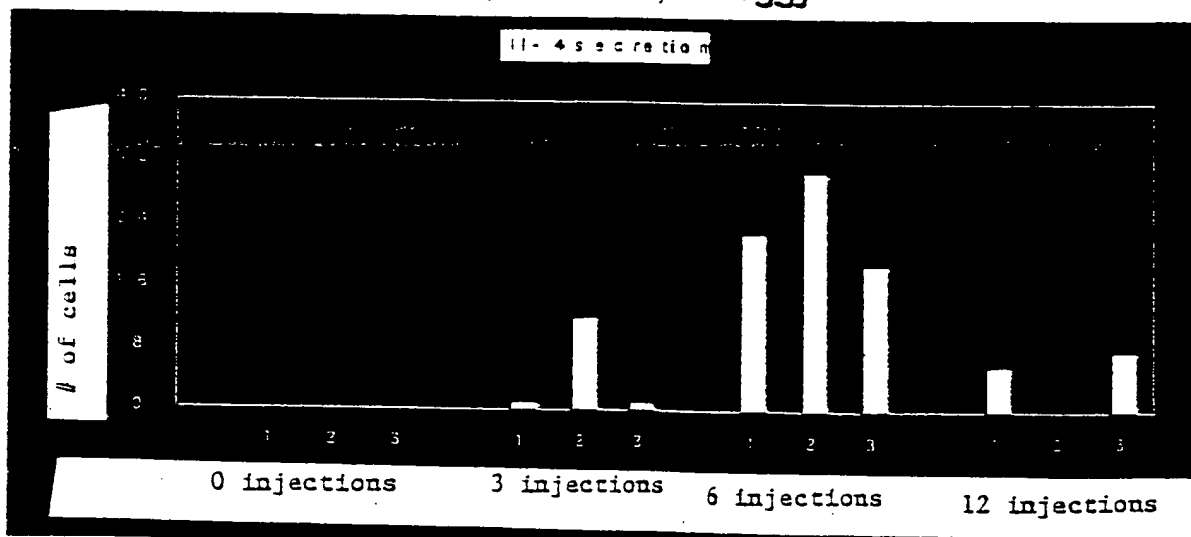
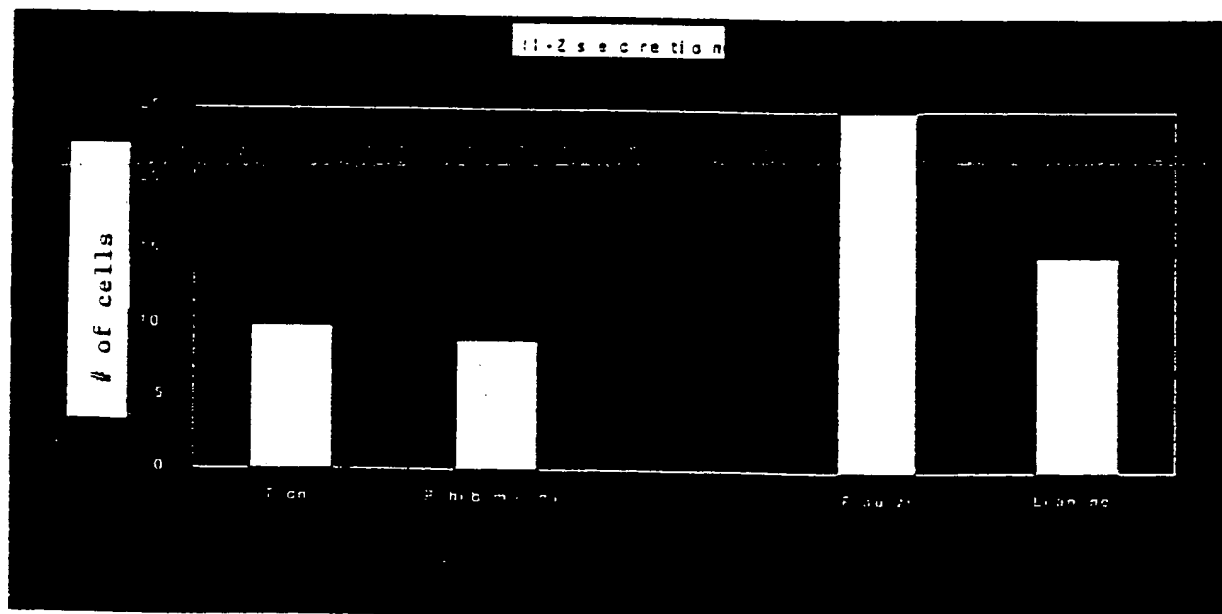
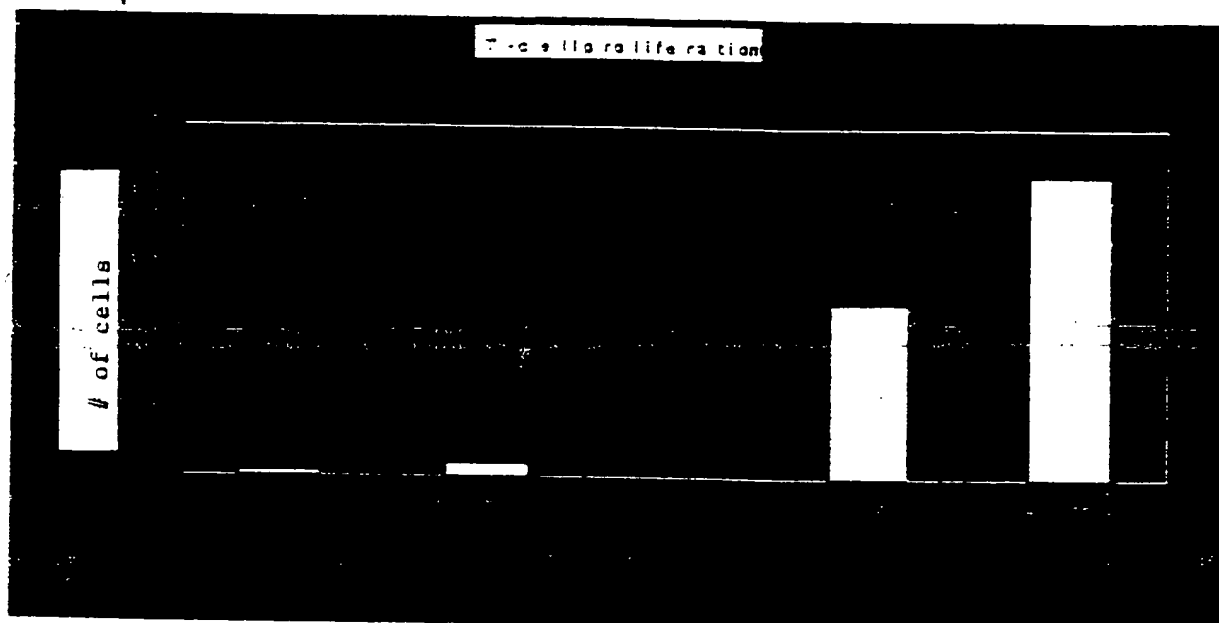


Fig. 50



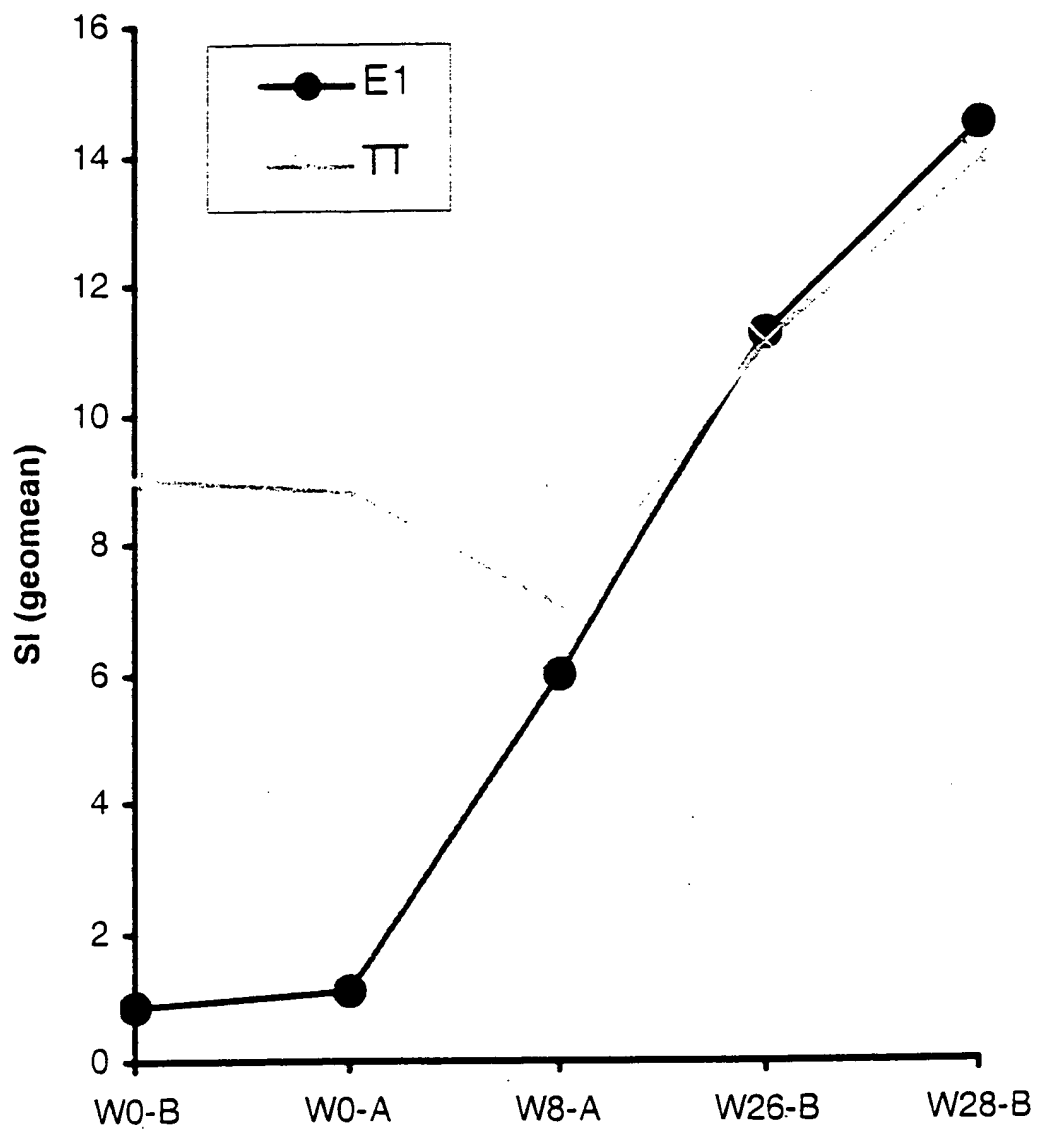


Fig 51

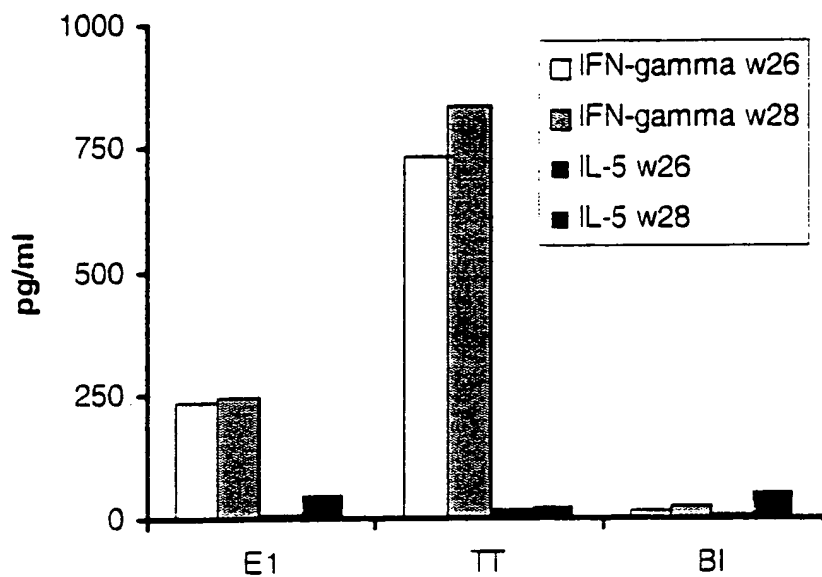
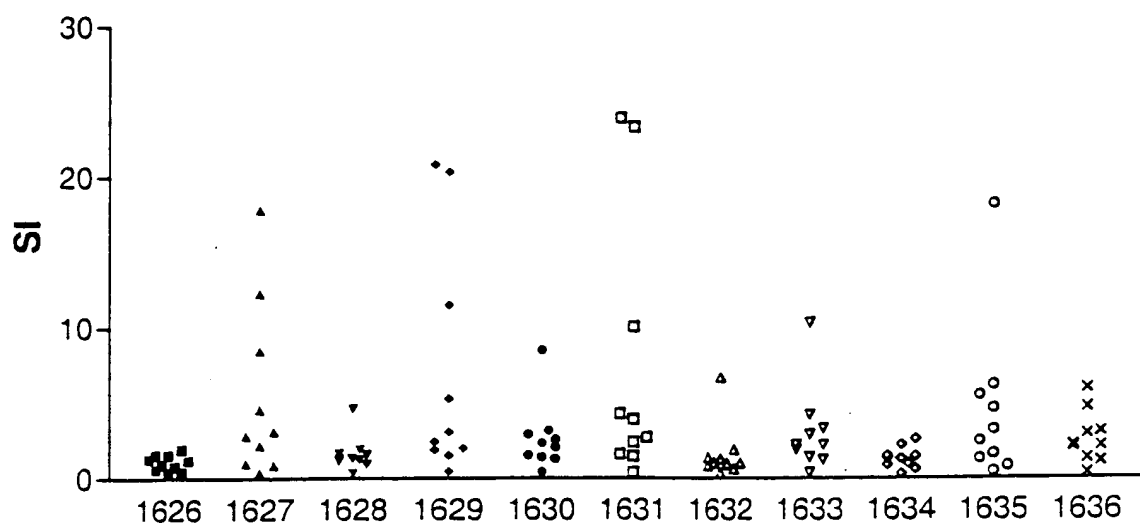


Fig 52



Fig 53

**vaccinated**



**controls**

